The Canadian Medical Association Journal

Vol. 58 JUNE, 1948 No. 6

THE USES OF STREPTOMYCIN IN UROLOGY*

John T. MacLean, M.D., Emerson Smith, M.D., Lloyd Bower, M.D. and Frederick Smith, M.D.

Montreal, Que.

PART I.—STREPTOMYCIN AND MOOGROL IN GENITO-URINARY TUBERCULOSIS

IT is desired to present the uses of streptomycin in the various aspects of urological cases under three sections, as the method of use and the principles underlying its use are entirely different in each section. This first section will be followed in later issues of this *Journal* by papers on (*a*) The Use of Streptomycin in Uretero-Intestinal Transplants, and (*b*) The Use of Streptomycin in Pyogenic Urinary Tract Infections including Prostatitis and Urethritis.

Hinshaw *et al.*[1] in a report on over 100 cases of various types of tuberculosis state that "The mycobacterium of tuberculosis is susceptible to streptomycin and that the course of the disease can be changed if an adequate dose is administered". It has been known for some time that the *M. tuberculosis* like the *M. lepræ* has a waxy cell wall, which protects the organism. Slotkin[2] concluded that if there was a substance which would dissolve this protecting waxy wall of the *M. tuberculosis* the organism might then be attacked by an antibiotic. He conceived the idea of dissolving this waxy wall with chaulmoogra oil and then giving the organism what would now be a lethal dose of streptomycin. He reported six cases so treated with apparently exceptionally good results.

During the past year we have had an unusual opportunity to study the possibilities offered by this method of treatment, and wish to present ten cases so treated. In all cases treated, moogrol which is the ethyl ester of hydnocarpus oil was used.

* From the Departments of Urology and Bacteriology, Royal Victoria Hospital, Montreal.

CASE 1

J.L., aged 36, male. This patient was admitted to the Royal Victoria Hospital on January 9, 1948, complaining of dysuria of two months' duration, and frequency, day every half-hour, night 3 to 5 times, also of two months' duration. He gave a history of having had an orchidectomy on the left side in 1927, in Russia, for tuberculosis. In 1935, an epididymectomy was done on the right side for tuberculosis. On the present admission, physical examination was essentially normal except for some induration in the right lateral lobe of the prostate. A roentgenogram of the chest showed Ghon tubercles in both upper lobes.

Laboratory data.—Urinalysis: pus xxx. Red blood cells occasional. Smear, positive for tubercle bacilli. Blood count: Hgb. 88%; white blood cells 6,400. Phenolsulphonpthalein excretion 65% in 2 hours. Non-protein nitrogen 23.4 mgm. %. Urine cultures negative for tubercle bacilli. Guinea pig inoculated with urine showed generalized tuberculosis.

January 10.—Cystoscopy showed moderate inflammation of the bladder mucosa with ulceration at the left ureteral orifice. Urine from the right ureter was normal. Urine from the left ureter showed many pus cells and a few red blood cells. Pyelograms showed irregular filling on the left with deformity of the calyces, typical of tuberculosis (Fig. 1).

Treatment.—January 16. Nephrectomy, left —a small amount of urine escaped into the wound. Pathological report—tuberculosis of the left kidney. Postoperatively the wound which was infected at the time of operation opened up widely. The patient was given 1 c.c. of moogrol and 1 gram of streptomycin intramuscularly daily for 18 days. In addition he was given local treatments of quartz lamp and ultra violet to the wound. There was rapid granulation in the wound following this treatment. He was discharged on March 6, with the wound still wide open. At this time he was voiding day 6, night 1 or 2 times. Urinalysis was entirely normal. Lowenstein cultures and guinea pig inoculations were not done at this time. One month later the wound was much smaller in size and was granulating well.

Conclusion.—Moogrol and streptomycin appeared to hasten the healing of a tuberculous nephrectomy wound.

CASE 2

D.B., aged 29, female. This patient was admitted to the Royal Victoria Hospital on November 2, 1947, complaining of a moderate degree of hæmaturia, colicky pain in the left loin; urinary frequency day 6 or 7 times; night 2 or 3 times and slight dysuria. She gave the following history:

November, 1940.—Tuberculous osteomyelitis of the 1st right rib with a tuberculous abscess of the chest wall; excision of the abscess with partial resection of the first and second ribs. September, 1941.—Tuberculous abscess of the right pectoral region and tuberculous osteomyelitis of the right second rib; excision of the tuberculous abscess and a portion of the rib. September, 1945.—Chronic appendicitis with appendectomy. October, 1946.—Right sided renal tuberculosis, with nephrectomy.

Physical examination was essentially normal.

Laboratory data on present admission.—Urinalysis: pus two plus; red blood cells plus; scattered epithelial cells. Guinea pig inoculated with urine, positive for tuberculosis.

Cystoscopy; the bladder mucosa was inflamed with scattered areas of hæmorrhage in the mucosa. The left pyelogram showed calyceal changes suggestive of tuberculosis. A guinea pig inoculated with urine from the left kidney developed multiple tuberculous lesions (Figs. 2 and 3).

Treatment.—This patient was given 1 c.c. of moogrol and 1 gram of streptomycin intramuscularly daily for 48 days. Guinea pigs inoculated with urine on November 15, November 24, and December 1, were all positive for tuberculosis. She was discharged from the hospital on December 24, 1947, at which time she was symptomatically greatly improved. The nocturia and frequency were improved. The bladder capacity had increased from 4½ to 9½ ounces. The urine still showed an occasional white blood cell and an occasional red blood cell.

Conclusion.—This case demonstrated both a clinical and symptomatic improvement following treatment with moogrol and streptomycin.

CASE 3

J.T., aged 53, male. This patient was admitted to the Royal Victoria Hospital on October 22, 1947. In December, 1939, he had had the right kidney removed for tuberculosis. On this admission he complained of frequency day/night every ½ hour/every ½ hour present for the past 7 years. He voided approximately 30 c.c. at each time. He also complained of bladder spasm 2 to 3 times a day for the past 3 months.

The physical examination was essentially normal.

Urinalysis showed scattered white blood cells; rare red blood cells. Non-protein nitrogen 31 mgm. % (Fig. 4).

Treatment.—This patient was given 1 c.c. of moogrol and 1 gram of streptomycin intramuscularly daily for 49 days. A cystoscopic examination 23 days after treatment was started showed a small contracted bladder of 30 c.c. capacity, with scattered areas of congestion. An intravenous pyelogram series on December 9, showed a left hydronephrosis and hydroureter (Fig. 4). This patient was discharged on December 12, with the frequency approximately the same and the bladder capacity unchanged. The bladder spasms had disappeared. Guinea pig inoculations of bladder urine, before, during, and after streptomycin failed to reveal any evidence of tuberculosis.

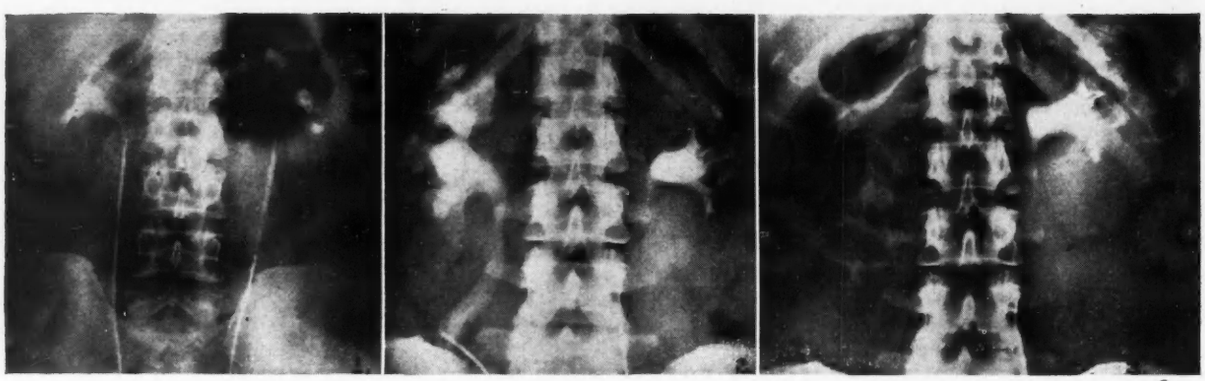


Fig. 1. (Case 1).—Retrograde pyelograms showing irregular filling on the left with deformity of the calyces. **Fig. 2.** (Case 2).—Preoperative pyelogram in 1946—showing advanced tuberculosis in right kidney. **Fig. 3.** (Case 2).—Left pyelogram, November, 1947—showing tuberculosis in left kidney (guinea pig positive).

Conclusion.—This case demonstrates as does Case 5 that there is little change to be expected from the use of streptomycin with moogrol in a small fibrosed bladder, the seat of an old, chronic inflammatory process.

CASE 4

F.L., aged 33, male. This patient was admitted to the Royal Victoria Hospital on April 8, 1948. He is included in this series because he demonstrates some very interesting features. He had been in the Royal Edward Laurentian Hospital in May, 1947, suffering from miliary tuberculosis (Fig. 5). At that time his sputum showed numerous tubercle bacilli.

Treatment.—In July, 1947, during the acute episode of miliary tuberculosis, the left epididymis became swollen and tender. The patient was given 1 gm. of streptomycin intramuscularly daily for a total of 102 days, as follows: July and August, 1947, 60 gm.; December 20 to January 21, 1948, 31 gm.; February 26 to April 7, 21 gm. The interesting thing is first the re-

markable improvement in the chest plate (Fig. 6), and secondly that the left-sided epididymitis is essentially unaltered from what it was at the commencement of treatment. Physical examination is normal. Gastric lavage has been negative on two occasions. The urinalysis shows 1 to 3 white blood cells per high power field. The intravenous pyelograms are normal. Orchido-epididymectomy was carried out on April 10.

Conclusion.—The improvement in the chest pictures is truly astonishing. And yet, strangely enough, the failure of the epididymis to respond to this intensive streptomycin therapy corresponds exactly with non-tuberculous infections in the epididymis. This raises the question whether the response of the tuberculous epididymitis to streptomycin would have been more complete if moogrol had been used along with the streptomycin.

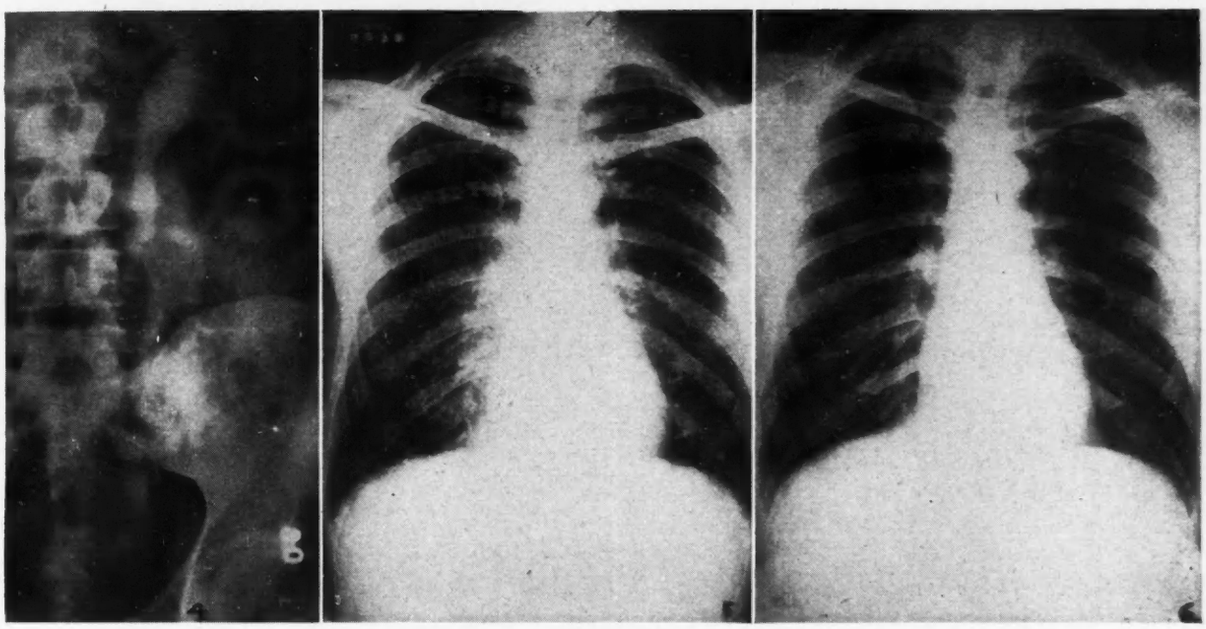


Fig. 4. (Case 3).—Advanced hydronephrosis and hydroureter on left side—9 years after right nephrectomy. Note small contracted bladder. **Fig. 5.** (Case 4).—Chest plate July, 1947, showing miliary pulmonary tuberculosis—sputum strongly positive for tubercle bacilli. **Fig. 6.** (Case 4).—March, 1948, after streptomycin therapy. No evidence of pulmonary tuberculosis.

CASE 5

H.K., aged 47, male. This patient was admitted to the Royal Victoria Hospital on October 21, 1947, complaining of frequency of urination, every 15 minutes during the day, and every hour during the night. In addition, he complained of terminal dysuria and a minor degree of hæmaturia. He gave a history of having had a right-sided nephrectomy in 1938 for renal tuberculosis, and five admissions in the interval for vesical tuberculosis and urethral stricture.

Physical examination was essentially normal.

Laboratory data.—Urinalysis: scattered white blood cells; red blood cells three plus. Repeated urine cultures negative for tubercle bacilli. Repeated guinea pig inoculations negative for tubercle bacilli. Blood Wassermann negative. Non-protein nitrogen 41.0 mgm. %.

Cystoscopy: The bladder was markedly contracted with generalized inflammation. The bladder capacity was 2 ounces.

Treatment.—This patient was given 1 c.c. of moogrol and 1 gm. of streptomycin intramuscularly daily for 30 days. There was no improvement in his symptoms. He was then given an instillation of 25% alcohol, and finally 95% alcohol into the bladder four days apart. He was discharged from the hospital December 1, with a urinary frequency of every hour day and night, and the bladder capacity unchanged. Guinea pig inoculations before and after streptomycin therapy were negative for tubercle bacilli.

Conclusion.—This patient with a small contracted fibrotic tuberculous bladder did not benefit from moogrol and streptomycin therapy.

CASE 6

G.G., aged 44, male. This patient was admitted to the Royal Victoria Hospital on March 23, 1948, complaining of frequency, day 8 to 10 times; night 4 or 5 times, of 2 years' duration; dysuria one year; and of a minor degree of hæmaturia on three occasions during the past year. In addition he complained of urgency of 2 years' duration, and of having passed small calculi on two occasions. Physical examination was essentially normal. The roentgenogram of the chest showed no evidence of tuberculosis.

Laboratory data.—Urinalysis: pus one plus; red blood cells rare. Urine culture, no tubercle bacilli found. Guinea pig inoculation positive.

Intravenous pyelogram series demonstrated a non-functioning kidney on the right side, with generalized calcification (Fig. 7). At cystoscopy, a granulomatous and œdematous mucosa was found about the right ureteral orifice. Three small ulcers were seen on the dome of the bladder.

Treatment.—Nephrectomy was performed on the right side. A tuberculous kidney showing extensive caseation was removed. The patient was given moogrol 1 c.c. and streptomycin 1 gm. intramuscularly daily. Fifteen days later the nephrectomy wound was completely healed and the patient was voiding every four hours during the day, and once at night. His urine was free of infection.

Conclusion.—In this case it is too early to evaluate how much of the improvement is due to chemotherapy, and how much is due to removing the reservoir that was feeding infection into the bladder.

CASE 7

Y.T., aged 38, female. This patient was admitted to the Royal Victoria Hospital on March 11, 1948. She had been under treatment for genito-urinary tuberculosis for several years. In 1942 she had had a calculus in the right kidney associated with pregnancy. In May, 1946, she had had a right-sided nephrectomy with removal of a tuberculous kidney. On this admission (March, 1948) she complained of intermittent hæmaturia one year; frequency, day 12 to 15 times; night 5 times, for four months, dysuria, and occasional suprapubic pain.

Physical examination was essentially normal.

Laboratory data.—Urinalysis: scattered pus cells. Red blood cells two plus. Urine culture negative for tubercle bacilli. Guinea pig inoculation negative. Phenolsulphonphthalein excretion 45% in 2 hours. Non-protein nitrogen 18.5 mgm. %; creatinine 1.39 mgm. %. Intravenous pyelogram showed a normal left kidney and normal pyelogram (Fig. 8).

Cystoscopy showed a generalized chronic inflammation with a granular trigonitis. There was slight hæmaturia following the introduction of 120 c.c. of fluid.

Treatment.—This patient was given 1 gm. of streptomycin and 1 c.c. of moogrol intramuscu-

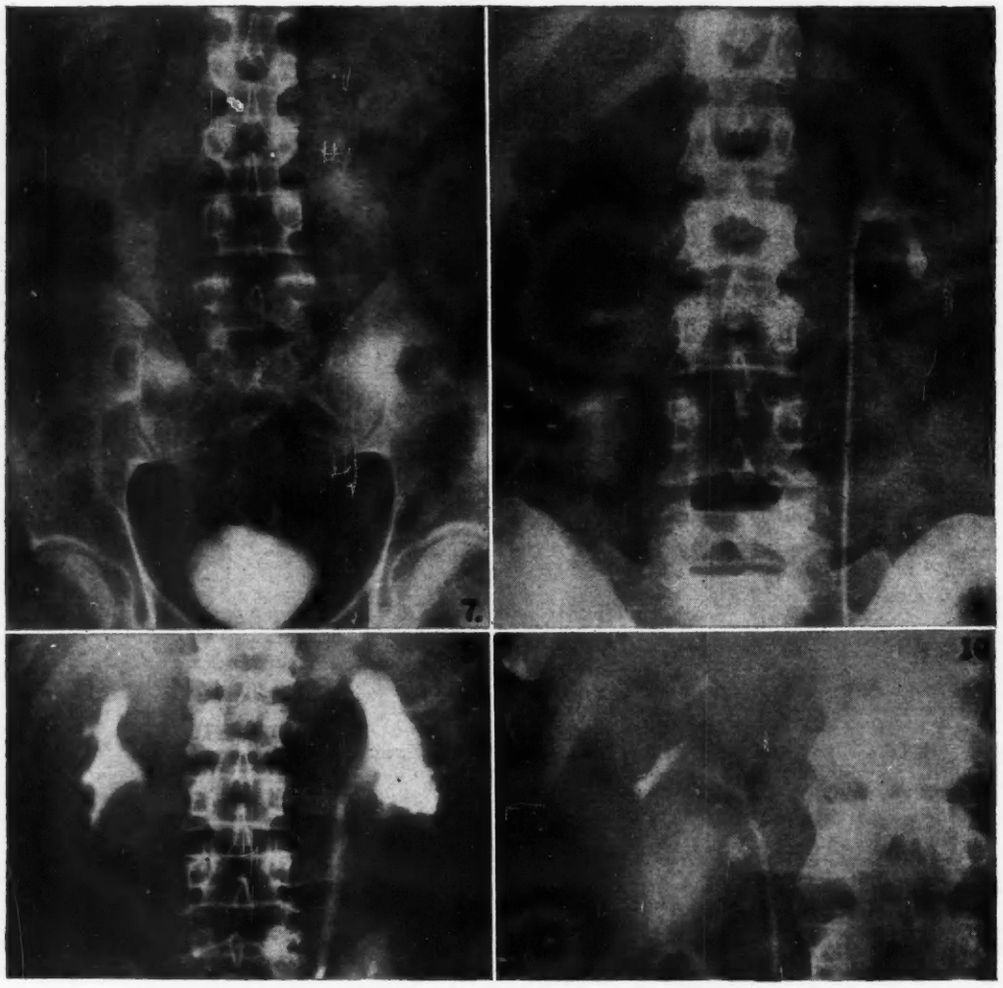


Fig. 7. (Case 6).—Multiple areas of tuberculous calcification in poorly functioning right kidney. Retrograde pyelogram showed left kidney to be normal. **Fig. 8.** (Case 7).—Intravenous pyelogram in March, 1948, showing normal left kidney. **Fig. 9.** (Case 8).—Bilateral renal tuberculosis with hydronephrosis and cavitation on left. **Fig. 10.** (Case 8).—Marked improvement in the right pyelogram four months after left nephrectomy, followed by streptomycin and moogrol therapy.

larly daily for 28 days (to date). Clinically she has improved considerably. The dysuria and suprapubic pain have disappeared. The bladder capacity has increased to 200 c.c. The frequency has been reduced to: day 4 times; night 1 or 2 times. There has been no hæmaturia.

Conclusion.—Although it is too early to accurately evaluate the results obtained in this case, there has been marked clinical improvement.

CASE 8

B.W., aged 42, male. This patient was admitted to the Grace Dart Home Hospital, August 8, 1947, with a history of having had pleurisy on the right side in 1930, and hæmoptysis in 1942. At that time a diagnosis of pulmonary tuberculosis was made at the Royal Edward Laurentian Hospital. The patient refused sanatorium treatment, merely rested for a while, and then returned to work. In January, 1947, the patient complained of rapid loss of 20 lb. in weight and extreme fatigue. In March he had another attack of hæmoptysis, and finally in August, was admitted to the Grace Dart Home Hospital, complaining in addition, of frequency, day 15 times; night 4 or 5 times, burning micturition and hæmaturia.

Physical examination revealed an emaciated male with advanced bilateral pulmonary tuberculosis. He also showed tenderness in the right costo-vertebral angle and an epididymitis on the right side. His blood count at this time showed red blood cells 2,790,000 and hæmoglobin 72%. The urine showed pus three plus and many tubercle bacilli on direct smear.

In September, a right epididymectomy was performed. On October 30, a cystoscopic examination showed an intensely inflamed and rugose bladder wall throughout. The left ureteral orifice was not œdematous but emitted spurts of very cloudy urine. On passing a catheter up the left ureter 40 c.c. of dirty thick urine was obtained. The urine obtained from the right side was clear. Guinea pig inoculations with the urine from each kidney were positive for tuberculosis. The pyelograms showed a completely destroyed kidney on the left side and some disease on the right (Figs. 9 and 10).

Treatment.—A concentrated effort was made to build the patient up physically and get him into condition for operation. On December 4, 1947, a nephrectomy was performed on the left side. The ureter was grossly infected and approximately 1 cm. thick. It was intended to do a nephro-ureterectomy, but the patient tolerated the procedure poorly, having a blood pressure of 10 mm. Hg. during the last 15 minutes of the operation, in spite of the fact that there was a minimal degree of blood lost. The kidney was therefore removed, and the grossly infected ureter left behind.

Postoperatively the patient did very well. He was given 1 c.c. of moogrol and 1½ gm. of streptomycin intramuscularly daily for 60 days. The wound healed *per primam.* In the intervening four months since operation he has gained 27 pounds in weight. His urinary symptoms have entirely disappeared with the exception of some frequency. A cystoscopic examination done on April 1, 1948, revealed an entirely normal-appearing bladder with a mild degree of median lobe prostatic intrusion (probably accounting for the frequency). The urine now shows a very rare white blood cell, and cultures of the urine are negative for tubercle bacilli.

Conclusion.—This is a case of bilateral and renal tuberculosis. It is interesting to note that with removal of the left kidney plus the treatment with moogrol and streptomycin, the gross infection in the left ureter appears to have looked after itself, and there is no longer any evidence of infection in the right kidney.

CASE 9

L.B., aged 24, male. This patient first came under observation in April, 1945, in the Ste. Annes' Military Hospital. At that time he had bilateral pulmonary tuberculosis, tuberculosis of the left knee joint, Pott's disease of the spine, tuberculosis of the right kidney with early pyelographic changes, and bilateral tuberculous epididymitis and prostatitis. It was felt that there was little to be gained by doing a nephroureterectomy on the right side because of the multiple lesions elsewhere. Sanatorium treatment seemed to be the treatment of choice. A bilateral epididymectomy was performed and the patient transferred to a sanatorium where he has remained ever since. During the intervening 3 years the pulmonary lesion has become quiescent, the Pott's disease of the spine has improved; but the tuberculous lesion in the right kidney has steadily progressed.

He was admitted to the Queen Mary Veteran's Hospital, March 1, 1948, at which time he had marked frequency, and burning on micturition. Urinalysis showed 60 pus cells per high power field, and many tubercle bacilli were found on direct smear.

Treatment.—A nephrectomy was done on the right side on March 3. The patient was given 1 c.c. of moogrol and 1 gm. of streptomycin for two days preoperatively. Postoperatively he was given 1 c.c. of moogrol for three days, and 2.5 gm. of streptomycin intramuscularly for seven days. The wound healed *per primam,* and his urinary symptoms completely disappeared. He was transferred back to the sanatorium March 31. At this time his urine showed only five white blood cells per high power field.

Conclusion.—This case is included in the series to demonstrate the remarkable improvement that can occur in the urinary symptoms following the removal of a tuberculous kidney. It is highly improbable that the moogrol and streptomycin given in this case contributed very much to the prompt recovery.

CASE 10

A.G., aged 37, male. This patient developed a tuberculous pleurisy on the right side in 1943. In November, 1944, he developed frequency, nocturia and urgency. Cystoscopy at this time revealed numerous tubercle-like

lesions about the right ureteral orifice, and a destructive lesion of the right kidney. In June, 1945, a nephrectomy was done on the right side, and a tuberculous kidney removed. In January, 1948, the patient complained of urgency and frequency and showed a moderate amount of purulent urethral discharge. Repeated smears of the urethral discharge were negative for tubercle bacilli. Cystoscopic examination showed chronic inflammatory changes in the bladder and posterior urethra. A diagnosis of chronic tuberculous prostatitis and seminal vesiculitis was made.

Treatment.—He was given 1 c.c. of moogrol and 1 gm. of streptomycin intramuscularly daily for 30 days. The frequency, burning on micturition, and urethral discharge completely disappeared. Prostatic fluid now showed epithelial cells, debris, and a very rare white blood cell.

Conclusion.—This case is included in the series to demonstrate an apparently successful outcome in a case of chronic prostatitis and seminal vesiculitis presumably tuberculous in origin. The normal course of the disease in such a case would be one of prolonged chronicity.

SUMMARY

In attempting to evaluate any type of therapy in cases of genito-urinary tuberculosis, it must be borne in mind that the greatest single characteristic of this type of tuberculosis is its *marked tendency to spread.* Further, it is a well known fact that removal of a tuberculous kidney alone without any chemotherapy at all, will often result in immediate relief of urinary symptoms and rapid healing of the bladder lesions.

In evaluating the effect of moogrol and streptomycin therapy on genito-urinary tuberculosis, one must therefore exercise reasonable caution.

It is realized that the number of cases presented is small, and does not necessarily establish incontrovertible proof. However, the observations are interesting, and we believe that there is sufficient evidence to indicate that by the use of moogrol 1 c.c. and streptomycin 1 gm. daily for one month, in cases of genito-urinary tuberculosis, certain benefits may ensue.

CONCLUSIONS

1. With the use of streptomycin and moogrol, there is definite clinical improvement at the end of the period of therapy in some cases of renal tuberculosis and pronounced improvement in others (*e.g.*, Cases 2 and 8).

2. Tuberculous epididymitis responds very slowly, if at all, to streptomycin therapy. This parallels exactly the failure of non-specific epididymitis to respond to penicillin therapy. The question may well be raised if this is due to failure to obtain an adequate concentration of the drug in the tissue concerned (Case 4).

3. There is little to be gained by giving moogrol and streptomycin therapy to patients with a small contracted tuberculous bladder, especially if the urine is negative for tubercle bacilli. The clinical symptoms are perhaps slightly improved, but the overall picture is unaltered (Cases 3 and 5).

4. Case 8 demonstrates a case of bilateral renal tuberculosis in which the more severely infected kidney was removed and the lesion in the other kidney healed following moogrol and streptomycin therapy.

5. Intensive therapy with moogrol and streptomycin appears to hasten the granulation and healing of grossly infected tuberculous wounds (Case 1).

6. The use of this combination in the treatment of tuberculous prostatitis and seminal vesiculitis offers interesting possibilities. In a case not reported in this series a large tuberculous abscess in the left seminal vesicle was deliberately incised and 8 c.c. of pus evacuated. The cavity of the seminal vesicle was filled with small pieces of gelfoam dipped in water, and then into dry crystals of streptomycin. In all, 2 grams of streptomycin was used. Another 2 grams of streptomycin was dusted into the perineal wound, and the wound closed tightly. The patient was given 1 c.c. of moogrol and 1 gram of streptomycin, daily postoperatively. He is progressing favourably and the wound has healed *per primam.* It is too early to predict the end result.

7. There was no demonstrable spread of infection during the period of observation in any of the ten patients treated.

8. The optimum dosage of moogrol and streptomycin, and the length of time over which this should be given, has not yet been established.

The authors wish to express their appreciation to Dr. Magnus Seng and Dr. A. B. Hawthorne of the Department of Urology, for permission to include their cases.

BIBLIOGRAPHY

1. HINSHAW, H. C., FELDMAN, W. H. AND PFUETZE, K. H.: *J. Am. M. Ass.*, **132**: 778, 1946.
2. SLOTKIN, G. E.: *J. Urol.*, **58**: 464, 1947.

DUPUYTREN'S CONTRACTURE

Stuart Gordon, M.B., M.S.(Tor.), F.R.C.S.[C.]

Toronto, Ont.

SINCE Dupuytren, in 1831, first established the fact that the palmar fascia and not tendon was involved in the disease which has, as a result, become known as Dupuytren's contracture, much has been written about it. Nevertheless, we still are not certain as to the factors responsible for the development of the disease, nor are we sure as to the nature of the pathological change. I wish to present to you certain facts as well as some impressions which have been gained from the study of some one hundred patients seen in the divisions of Plastic Surgery at the Toronto General and Christie Street Hospitals, of whom I have operated upon 51.

Anatomy.—The superficial palmar fascia consists of a central thickened portion, and two thinner lateral portions covering the thenar and hypothenar eminences. The central portion is a continuation of the palmaris longus. To this is added a layer extending distally from the anterior carpal ligament which fuses with the superficial portion about an inch distal to the ligament. This central portion—the portion almost always involved in Dupuytren's contracture—fans out from its rather narrow origin into, usually, 4 thickened longitudinal bands joined by thinner, more or less transverse fibres which lie deep to them. Three main septa project dorsally at right angles from the fascia to join the anterior interosseous fascia and so form fascial tunnels for the passage of nerves, vessels and tendons. The most radially placed septum extends further proximally than the other two. From the superficial surface of this central portion many short fibres extend at right angles to connect the fascia to the skin. Distally, the bands thin out, split into two and pass over the anterior and lateral surfaces of the fingers, where they fuse with the skin over the first and second phalanges.

Pathology.—The exact pathological nature of the lesion is still an open question. Early, and some recent, opinion has favoured a chronic inflammatory process as the basic change. Clay believes the lesion to be a definite fibroma, *i.e.*, a benign neoplasm. Certainly, if a tumour is a local tissue overgrowth, independent of the laws governing the rest of the body, and serving no useful purpose, it seems to me logical to regard the disease as neoplastic. Part of the difficulty may be that we have in Dupuytren's contracture a pathological change developing in a degenerated structure. The material from our cases is being studied and I hope that the results of this study will be presented at some time in the future.

Etiology.—The etiology of the lesion is unknown. Heredity (Table I) is one of the many suggested factors that appear to have some realistic basis. Koch found 10 positive family histories in 13 physicians or members of physicians' families suffering from the disease. Of 37 personal cases in which records would seem to be accurate, only 4 gave a positive family history. The male parent had had the disease in 2 instances, the mother in 1. A brother had a similar lesion in the fourth instance. Couch has recorded an interesting example of the disease occurring in identical twins.

TABLE I.

		Family history	
	Cases	*Positive*	*Negative*
McWilliams	24	2	22
Janssen	16	0	16
Davis	40	5	35
Keen	198	50	148
Gordon	37	4	33
	315	61	254

It may well be, as Manson has pointed out, that the part heredity plays does not show fully since many die before senescent hereditary defects appear.

Trauma has been regarded as a responsible factor since the disease was first described. Nevertheless, the disease appears to be commoner in non-workers than in workers (Table II).

TABLE II.

	Cases	*Workers*	*Non-workers*
Black	131	63	68
Byford	38	24	14
Keen	123	49	74
Kanavel, Koch and Mason	29	10	19
Davis and Finesilver	40	20	20
Meyerding	273	123	150
	634	289	345

Oller pointed out in 1929 that it was comparatively rare in those doing manual labour. An occasional patient is seen in whom trauma appears to have played a part. Usually the individual has been attempting to lift a heavy weight and has suddenly developed a sharply localized stinging pain in the palm. This area has remained tender on pressure, and within a month or so a typical nodule has appeared. The continuity of the story forces conviction.

Many diseases are listed in the literature as being associated with, or influencing, Dupuytren's contracture. Gout, arthritis, endocrine deficiencies, diabetes mellitus, lead poisoning, ulnar nerve lesions, syphilis, ganglionitis, cervical rib and coronary thrombosis are among those mentioned. Powers believes that Dupuy-

tren's contracture is not a clinical entity but rather a diagnostic sign. The causative factor, in his opinion, is past or present visceral disease producing irritation of the sympathetic nervous system. Kehl, discussing 6 cases of Dupuytren's contracture following coronary occlusion, concludes that the palmar lesion appears to be a complication of or sequel to the cardiac condition. On the other hand Johnson, reporting 39 instances of trophic changes occurring in the hands of 178 consecutive cases of myocardial infarction, does not mention Dupuytren's contracture. Nor does Evans in a discussion of reflex sympathetic dystrophies. In my opinion, coincidence probably accounts for the suggested association of Dupuytren's contracture with other syndromes. At the very least we must return the Scottish verdict of "not proved". Of 40 personal cases 30 had no evidence of other disease, 1 had an ulnar nerve lesion, 5 had arthritis, 1 had prostatic enlargement, 1 had

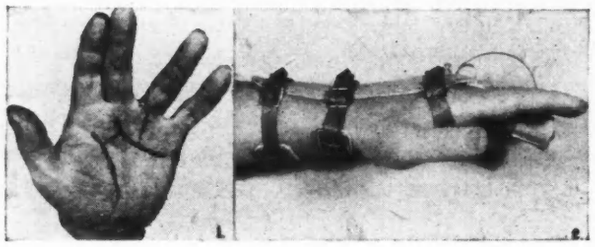


Fig. 1.—The routine incision for opening the palm is shown. The incision used for operating upon an extension to the fourth finger is indicated. **Fig. 2.**—The extension splint used to improve extension of a finger (or fingers).

degenerative heart disease and 2 had healed pulmonary tuberculosis.

Incidence.—Dupuytren's contracture is not a rare disease. Its prevalence is difficult to ascertain. Ayre reported 64 instances in 486 Veterans' Guard of Canada. Davis and Finesilver found 7 lesions in 641 old people in the Baltimore City Hospital. Noble and Smith noted 70 cases in 700 inmates of London workhouses, and 40 cases in 1,000 soldiers. Anderson examined 2,600 persons and found 33 suffering from the disease. Byford found 37 in 1,106 persons. Thus figures from over 1 to 13% are to be found in the literature. Dupuytren's contracture caused 70 admissions of 2,177 to the Plastic Division at Christie Street Hospital during 1945, 1946 and the first 6 months of 1947.

Clinical course.—The disease may occur in an acute or chronic form: the latter is by far the commoner. I have seen the acute form twice. The hand becomes swollen, stiff and painful. Inflamed areas appear on the palm which are later the sites of thickening.

TABLE III.

	Numbers	*Right*	*Left*	*Bilateral*
Hume	118	57	21	40
Anderson	39	10	5	24
Black	240	89	47	104
Byford	38	9	4	25
Costhilles	77	14	8	55
Kanavel, Koch and Mason	29	4	8	17
Keen	184	58	23	103
Scholle	54	28	8	18
Davis and Finesilver	40	8	6	26
A. A. Davis	31	7	6	18
Meyerding	273	69	29	175
Gordon	50	12	4	34
	1,173	365	169	639

The usual chronic form develops over months or years and may show exacerbations and remissions. Typically a painless nodule appears just distal to the distal transverse crease opposite the ring finger. It may gradually produce a small funnel-like depression in the skin. Quiescent for months or years, the thickening gradually extends proximally and distally along the palmar fascia, slowly limiting extension of the ring finger. A similar lesion may now appear opposite the fifth finger. Further interference with function may be negligible or extension is lost progressively until the fingers are held fully flexed. By this time the mid, and probably the index fingers are involved. When the patient reports for treatment bilateral involvement is the rule. If one hand only is affected, it is usually the right (Table III).

TABLE IV.

	Cases	*Thumb*	*Index*	*Mid*	*Ring*	*Little*
Anderson	39	4	3	22	39	28
Byford	38	4	1	10	35	18
Kanavel, Koch and Mason	29	4	3	9	31	27
Noble and Smith	70	1	6	10	42	30
Keen	214	11	24	73	199	165
Scholle	54	1	5	9	45	28
Davis and Finesilver	40	3	6	14	40	43
A. A. Davis	31	0	0	5	27	26
Gordon	50	0	2	18	61	40
	565	28	50	170	519	405

While the majority of cases complain only of a painless deformity, some do have tenderness particularly on pressure. A few are troubled by cramps which may be more marked at night. Others suffer stiffness in the hand, most marked on wakening. Numbness, itching,

and aching are complained of in a few instances. The lesion may develop in the plantar fascia. In my series, such a lesion was seen twice in association with a palmar lesion, and once as a separate entity.

TABLE V.

	Cases	*Males*	*Females*
Keen	227	187	40
Anderson	39	25	14
Black	240	221	19
Byford	38	35	3
Kanavel, Koch and Mason	29	27	2
Davis and Finesilver	40	35	5
Noble and Smith	11	10	1
Daescher	18	17	1
Janssen	16	15	1
Costhilles	17	16	1
A. A. Davis	31	30	1
Gordon	51	46	5
	757	664	93

Dupuytren's contracture occurs more commonly in males, there being slightly more than 7 males to 1 female with the disease (Table V). The lesion is seen most often between the ages of 40 and 60.

Treatment. — Not all those suffering from Dupuytren's contracture require active therapy. A symptomless lesion which is not becoming worse need not be treated but should be watched. Pain, soreness and interference with function, particularly in a lesion which is progressing, indicate the need for treatment.

liminary to such excision. No operative interference should be done during the acute phase or during an exacerbation. All cases requiring operation should have the palmar fascia completely excised. If skin is hopelessly involved, it should be excised and replaced by a thick dermatome or a free full thickness graft. Grafting was necessary in 11 of 62 operations.

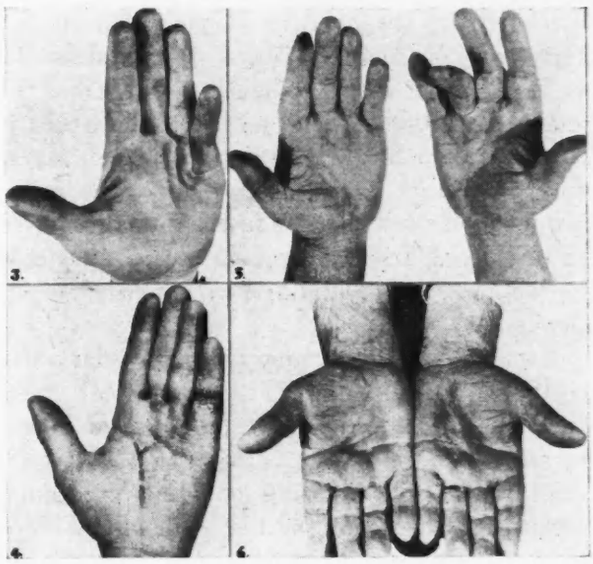


Fig. 3.—Typical preoperative appearance (February 27, 1946). **Fig. 4.**—Postoperative photograph taken March 21, 1946. **Figs. 5 and 6.**—Another illustrative case. The lesion in the left hand was early, but progressing. Preoperative photograph December 17, 1945; postoperative April 2, 1946.

TABLE VI.

		AGE OF ONSET					
	Cases	*Under* 30	30 *to* 39	40 *to* 49	50 *to* 59	60 *to* 69	70 *to* 79
Nichols	45	1	7	6	16	12	3
Kanavel, Koch and Mason	29	4	6	11	5	3	..
Costhilles	60	9	6	9	21	15	..
Scholle	54	8	9	12	15	10	..
Davis and Finesilver	35	5	9	12	6	3	..
Gordon	70	10	15	22	16	6	1
	293	37	52	72	79	49	4

Treatment is surgical. Radiation therapy, the injection of humanol, and the exhibition of thyroid extract have been tried but improvement has been slight or transitory and their value has not been established. Surgical treatment consists in doing either a multiple subcutaneous fasciotomy or completely excising the palmar fascia. The former was advocated by Adams in 1890 and as recently as 1932 Davis wrote: "It remains an operation of considerable value, perhaps of greatest value . . .". In my opinion this purely palliative procedure should be done only if the patient is unable, for physical reasons, to have the palmar fascia excised; or as a pre-

Operation is best done under general anæsthesia. A pneumatic tourniquet is placed above the arm and pumped to 250 mm. pressure after the arm has been elevated to empty the veins by gravity. The incision illustrated in Fig. 1 has become routine. Raising the two flaps gives complete access to the fascia. The short cross incision should not be over, but to one or other side of the third metacarpal. It will be noted that the main incisions are placed in flexion lines. There is sound reasoning for this, since, as Wood Jones has pointed out, flexion lines indicate "points of comparative skin rest". If the lesion extends into a finger (or fingers) the

incisions should be so placed that there will not be interference with joint movement at a later date.

Once the skin has been elevated, dissection of the fascia is started at or just beyond the distal border of the anterior carpal ligament. The portion of the palmar fascia arising from the palmaris longus is divided and turned down. This brings into view that portion of the fascia arising from the anterior carpal ligament. A transverse cut is made across this fascia and it is also turned distally, being gently freed by sharp dissection at the sides and underneath. Just distal to the point where these two layers fuse, dissection is commenced along the radial border of the fascia. The fascia is then removed in one piece, from the radial to the ulnar side of the hand and including any extension to the fingers.

Removal in this manner with the sharp dissection in the direction of the important structures in the palm, lessens the danger of injury to any of them. Only twice have I divided a digital nerve in carrying out this procedure. Immediate suture of the nerve should be done whenever such an accident occurs. The digital nerve is almost always displaced by extensions of the lesion to the finger; occasionally as far as the opposite side of the finger.

All blood vessels perforating the fascia noted while the skin is being elevated are caught with forceps and ligatured with fine plain catgut. Once the fascia is removed, obviously divided vessels are tied off with catgut. Gauze wrung out of normal saline is then packed into the operative area and firmly held while the tourniquet is released. After a minute or so the gauze is removed slowly from the base of the palm distally and all bleeding vessels caught and ligated. Oozing points are controlled with the electro-cautery. Great care should be taken to prevent the development of a postoperative hæmatoma. Once bleeding is controlled the tourniquet is re-applied and the incision closed with interrupted silk to ensure accurate approximation of the skin edges. A pressure dressing is applied, the fingers as a rule being kept free. Once the dressing is on, the tourniquet is removed.

The patient is encouraged to move the fingers as soon as he is awake. The dressed hand is elevated for 48 hours. At the end of 24 hours the dressing is removed. An hæmatoma should be evacuated. The pressure dressing is reapplied and remains in place for another week. It is then replaced by an ordinary dry dressing. As the skin of the palm heals slowly stitches are not removed until the 18th or 21st day. If the skin edges are not completely healed, the hand is kept relatively quiet until they are. When healing has taken place, the palm is usually thicker than normal and neither complete flexion nor extension are possible. Physiotherapy is then commenced and continued until full return of function occurs, or until improvement ceases, usually 2 to 3 months.

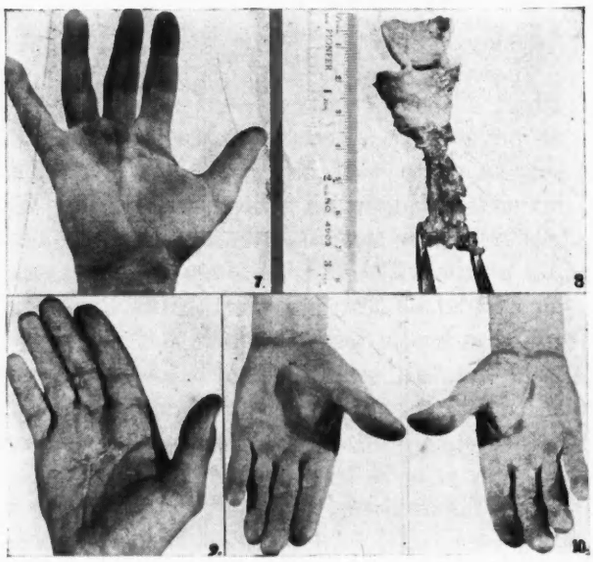


Fig. 7.—Marked involvement of the skin. The operative specimen, including skin from the palm and the palmar surface of the proximal phalanx of the mid finger, is shown (Fig. 8). The result after excision followed by dermatome grafting is seen in Fig. 9. Photographs were taken October 20, 1945, October 22, 1945, March 19, 1946. **Fig. 10.**—March 10, 1947, shows a band of subcutaneous thickening, from the base of each thumb medially and distally. No change in the lesion up to October, 1947.

It will be noted that during the treatment, the hand has not been splinted. Hands that are the site of a Dupuytren's contracture show a very definite tendency to stiffen when splinted. This applies particularly to the metacarpo-phalangeal joints, but is true in lesser degree of all the joints of the hand. During the period of physiotherapy, however, the intermittent use of a dorsal traction splint may aid when extension is unusually slow in returning.

RESULTS

Forty cases have been followed for from 1 to 12 years. Twenty-six may be classed as

excellent results, 7 good, 3 are graded fair in that while the lesion has been removed, function has only been improved slightly. One was, and is, a poor result, the condition of this hand when last seen being worse than prior to operation. There have been 3 recurrences. The first was due to inadequate excision in that only the involved portion was removed. The lesion reappeared 19 months after operation and at the second operation considerable palmar skin had to be removed with the palmar fascia. The result today, 17 months after the last operation, is excellent. The second recurrence I am unable to account for as I had done what I believed to be an adequate operation. Recurrence was evident 11 months after operation. He has just left hospital with a complete range of movement in his hand following a second operation. The third case is, perhaps, incorrectly labelled as a recurrence. He reported for examination about 19 months after his operation with thickening and some tenderness in the web between each thumb and base of index finger. The palmar area of each hand is otherwise free of any evidence of Dupuytren's contracture.

Campbell, working at Christie Street Hospital, has shown that part of the gripping power of a hand is lost as a result of the excision of the palmar fascia. This may amount to as much as 25% of the normal power.

CONCLUSION

Dupuytren's contracture is a fairly common lesion of the hands and is occasionally seen in the feet. Its etiology is unknown; its pathology questionable. It is commonest in males, and develops most frequently between the ages of 40 and 60. When first seen clinically, both hands are involved in the majority of instances; if only one hand is involved, it is usually the right. Finger involvement occurs in the 4th, 5th, 3rd, 2nd and thumb, in that order, the 4th being involved 10 times more frequently than the 2nd. The only satisfactory treatment is the excision of the palmar fascia, together with hopelessly involved skin. Skin replacement can be done satisfactorily with a thick dermatome graft. A good result may be expected in 85% of cases.

Illustrations from the Medical Art Department, Christie Street Hospital, Department of Veterans' Affairs.

BIBLIOGRAPHY

1. AYRE, W. B.: *Canad. M. A. J.*, **54**: 158, 1946.
2. BLACK, K.: *Brit. M. J.*, **1**: 326, 1915.
3. BUNNELL, S.: Surgery of the Hand, J. B. Lippincott Co., 162, 1944.
4. CAMPBELL, H. H.: Personal communication.
5. CLAY, R. C.: *Ann. Surg.*, **120**: 224, 1944.
6. COUCH, J. H.: *Canad. M. A. J.*, **39**: 225, 1938.
7. DAVIS, A. A.: *Brit. J. Surg.*, **19**: 539, 1932.
8. DAVIS, J. S. AND FINESILVER, E. M.: *Arch. Surg.*, **24**: 933, 1932.
9. EVANS, J. A.: *Surg., Gyn. & Obst.*, **82**: 36, 1946.
10. HUTCHINSON, J.: *The Lancet*, **1**: 285, 1917.
11. JOHNSON, A. C.: *Ann. Int. Med.*, **19**: 433, 1943.
12. KANAVEL, A. B., KOCH, S. L. AND MASON, M. L.: *Surg., Gyn. & Obst.*, **48**: 145, 1929.
13. KEHL, K. C.: *Ann. Int. Med.*, **19**: 213, 1943.
14. KOCH, S. L.: *J. Am. M. Ass.*, **100**: 878, 1933.
15. MANSON, J. S.: *Brit. M. J.*, **2**: 11, 1931.
16. MEYERDING, H. W.: *Arch. Surg.*, **32**: 320, 1936.
17. OLLER: Quoted by Davis and Finesilver.
18. POWER, H.: *J. Neurol & Mental Dis.*, **80**: 386, 1934.
19. STEINBROCKER, O.: *Am. J. Med.*, **3**: 402, 1947.
20. WOOD JONES, F.: The Principles of Anatomy as Seen in the Hand, Baillière, Tindall & Cox, London, **75**: 83, 1941.

RELATIONSHIP BETWEEN IMPAIRMENT OF LIVER FUNCTION AND PREMATURE DEVELOPMENT OF ARTERIOSCLEROSIS IN DIABETES MELLITUS*

I. M. Rabinowitch, M.D.

Montreal, Que.

ARTERIOSCLEROTIC disease of the heart, arteries and kidneys now accounts for approximately twice as many deaths amongst diabetics as all other causes of death combined. Arteriosclerosis is essentially a disease of people approaching and past middle life. Diabetes, though it occurs at all ages, is also essentially a disease of this type. Diabetics now also live much longer than before the advent of insulin. A high incidence of deaths from arteriosclerosis is, therefore, to be expected amongst diabetics. That this, however, does not alone explain the high mortality from arteriosclerosis may be clearly seen by comparing the causes of death among diabetics with those among non-diabetics according to age. These, particularly autopsy data, show that arteriosclerotic disease of the heart, arteries and kidneys is more common among diabetics than among non-diabetics at all ages. The findings of Root, Bland, Gordon and White[1] are an example. In a comparative study of 349 diabetic and 3,400 non-diabetic autopsies, the incidence of coronary occlusion, expressed as percentage of the total number of autopsies, was definitely greater in the diabetics than in the non-diabetics in all age groups investigated. The diabetic data were obtained in a clinic for

* Part of an address delivered before the Osler Clinical Society, University of Vermont, College of Medicine, Burlington, Vt., March 26, 1948.

diabetes. That this was not an exceptional experience, however, may be seen in the findings of Lisa, Magiday, Galloway and Hart[2] which reflect a general hospital experience with the usual percentage of admissions of diabetes. According to this study, arteriosclerosis is not only more common in the diabetic than in the non-diabetic at all ages, but that it appears at an earlier age and is more frequently severe.

Confirming these experiences there are the vital statistics. As an example, in Table I, are shown (*a*) the number of deaths from all causes and (*b*) the percentage of these deaths from "disease of the coronary arteries and angina pectoris" in the age periods 30 to 39 and 40 to 49 years in the general population of the United States in 1940, compared with the above-mentioned post-mortem findings of Root, Bland, Gordon and White in diabetics and non-diabetics. It will be noted that the percentages of deaths from "atherosclerosis with narrowing and occlusion" of the coronary arteries among the non-diabetics reported by Root and his associates agree very closely with the percentages from "disease of the coronary arteries and angina pectoris" in approximately the same age groups in the general population of the United States. The vital statistics of 1940 were purposely selected rather than the latest available since they corresponded approximately to the year in which Drs. Root, Bland, Gordon and White published their findings.

The optimistic view expressed by Dr. Joslin eleven years ago has, unfortunately, not been supported by subsequent experiences even in his own clinic. In 1937, Dr. Joslin[3] wrote "The postponement of premature arteriosclerosis has already begun. No longer does the statement hold that arteriosclerosis can be found post-mortem in all cases of diabetes of five years' duration". By then, Shields Warren[4] had found at autopsies at the Joslin Clinic four cases of diabetes of over 5 years' duration free from arteriosclerosis. As the writer, however, has shown[5] by analysis of the data of the Joslin Clinic since then, the occurrence of these four cases was probably accidental. In fact it appeared that the incidence of premature arteriosclerosis in the Joslin Clinic had actually increased. According to Priscilla White,[6] in the case of children, it would appear that it is "nearly inevitable". With this Dolger's[7] experiences are in complete agreement. Determination of the factors which contribute to the excess incidence of arteriosclerosis is, thus, one of the most urgent needs in present-day management of diabetes.

TABLE I.

INCIDENCE OF DISEASE OF THE CORONARY ARTERIES IN DIABETICS AND NON-DIABETICS ACCORDING TO POST-MORTEM EXAMINATIONS, AND MORTALITIES FROM DISEASE OF THE CORONARY ARTERIES IN THE GENERAL POPULATION, ACCORDING TO VITAL STATISTICS REPORTS ADJUSTED FOR AGE.

Age (years)	*Diabetes mellitus**			*No diabetes*						
				*Post-mortem examination**				*Vital statistics***		
	Number of cases	*Atherosclerosis with narrowing and occlusion*		*Number of cases*	*Atherosclerosis with narrowing and occlusion*		$\frac{a}{b}$	*Number of cases*	*Disease of the coronary arteries and angina pectoris*	
		No.	*% (a)*		*No.*	*% (b)*			*No.*	*%*
31-40†	13	3	23.0	340	10	2.9	7.9	76,249	2531	3.3
41-50‡	40	12	30.0	526	56	10.6	2.8	125,285	10168	8.1

*Root, H. F., Bland, E. F., Gordon, W. H. and White, P. D.: *J. Am. M. Ass.* **113:** 27, 1939.
**Vital Statistics of the United States, Pt. I, Table 11 (p. 210-252) 1940.
†Vital Statistics age periods 30 to 39 years.
‡Vital Statistics age periods 40 to 49 years.

DURATION OF DIABETES

It has been known for some time that duration of the diabetes is an important etiological factor. In 1930, Shields Warren[8] wrote "I have yet to see at autopsy a diabetic or to read the protocol of a diabetic whose disease lasted five years or more free from arteriosclerosis, regardless of age". The extent to which duration of the diabetes is a factor was shown by the writer[5] by correlation of the data in Tables 29 and 44

in the 7th edition of Joslin's *Treatment of Diabetes Mellitus*.[6] The chart then constructed is reproduced in Fig. 1. When this was shown to Dr. Joslin, he pointed out* that the parallelism between the duration of the diabetes and the percentage of deaths from cardio-vascular-renal disease would have been still more striking had the data included "our children who are living into the 15 and 20 year zones of duration and beginning to develop hypertension and cardio-vascular complications".

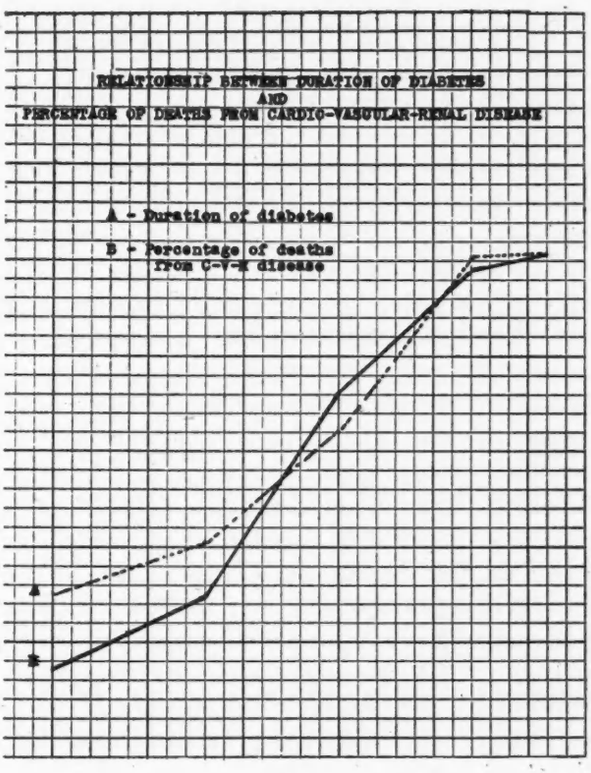


Fig. 1

(RABINOWITCH, I. M.: *Canad. M. A. J.*, 51: 300, 1944.)

If the duration of the diabetes was the only factor in the premature development of arteriosclerosis, the condition would have to be accepted as inevitable. That much can be done at least to postpone the premature development of arteriosclerosis in the diabetic was clearly shown by the writer[9] in a small group of cases in 1935. Of 50 patients who had had diabetes for an average of 5 years, 36 were still free from this complication. These were not post-mortem experiences. The method, however, which was employed to detect arteriosclerosis in these cases was shown to have an accuracy of, approximately, 85%, compared with the accuracy of post-mortem examinations.[10] In a later study[5] of another group of 50 cases with the diabetes of 10 years' average duration, 27 showed no arteriosclerosis, and, in a more recent study,* of 50 cases with the diabetes of 15 years' duration, 19 showed no arteriosclerosis—an incidence of 38%.

It is to be noted here that the individuals in the two subsequent studies — 5 and 10 year groups—were not entirely the same as in the first study; nor were they strictly comparable with each other, for two reasons: firstly, deaths had occurred in each group and, secondly, as in the first group of cases, it was necessary to exclude individuals who, at the end of the period of observation, were over age 50 years and, therefore, amongst whom a high incidence of arteriosclerosis would be expected independent of the diabetes. The purpose of these reports was merely to demonstrate the fact that of a given number of diabetics, with the disease of 5, 10 and 15 years' duration and still under age 50 years, an appreciable percentage was still free from arteriosclerosis, thus proving that, as a result of changes in the treatment of diabetes, the above-mentioned 5-year rule no more holds.

DEGREE OF CONTROL OF THE DIABETES

In addition to the duration of the diabetes, another factor which must now be considered as possible causes of the premature development of arteriosclerosis is the degree of control of the diabetes. The extent to which this was a factor in the past is not known, since, as stated, all diabetics, regardless of the control of the disease, had developed arteriosclerosis at the end of 5 years. That control of the diabetes is an important factor is suggested from the data shown in Table II in which is briefly summarized the relationship noted between the degree of control of the diabetes and the presence or absence of arteriosclerosis in the above-mentioned 5, 10 and 15 year groups of cases. The degree of control of the diabetes is expressed in terms of the Control Index.[9]

It will be noted that, regardless of the duration of the diabetes, the average control of the diabetes was poorer amongst those who had developed arteriosclerosis than amongst those who had escaped this complication. From a study of 100 diabetics observed for 10 years or more, Richardson and his associates[11] concluded that

* Personal communication.

* Reported at the New York Academy of Medicine, January 2, 1947.

constant and adequate control of the diabetes with insulin and relatively high carbohydrate diet tends to prevent premature arteriosclerosis.

SEVERITY OF THE DIABETES

It will also be noted that the percentage of individuals with arteriosclerosis in each of the 5, 10 and 15-year groups was higher in the insulin than in the non-insulin group. This suggested that the severity of the diabetes was a factor. Opposed to this is the common finding

TABLE II.

RELATIONSHIP BETWEEN DEGREE OF CONTROL OF DIABETES (CONTROL INDEX), DURATION OF DIABETES AND PREMATURE ARTERIOSCLEROSIS.

Duration of diabetes	*Group*	*Whole group*			*Arteriosclerosis**					
					Present			*Absent*		
		N	n	M	N	n	M	N	n	M
5 years	Whole	50	819	1.94	14	253	1.53	36	566	2.12
	Insulin	16	327	1.69	5	121	1.41	11	206	1.86
	No insulin	34	492	2.30	9	132	1.66	25	360	2.26
10 years	Whole	50	1460	2.09	23	597	1.88	27	863	2.12
	Insulin	36	1061	1.96	19	492	1.84	17	569	2.06
	No insulin	14	399	2.21	4	105	2.11	10	294	2.25
15 years	Whole	50	2055	2.04	31	1186	1.91	19	869	2.23
	Insulin	32	1491	2.12	21	875	2.01	11	616	2.28
	No insulin	18	564	1.85	10	311	1.64	8	253	2.11

N = Number of subjects

n = Number of tests

M = Average control index

(For calculation of control index, see *Ann. Int. Med.*, **8**: 1436, 1935.)

*For methods of detection, see *Ann. Int. Med.*, **7**: 1478, 1934.

of advanced heart disease in diabetics who require slight restriction of diet only, in order to keep the urine free from sugar and the blood sugar normal. That the severity of the diabetes is probably a factor only to the extent that the diabetes is more difficult to control in the severe than in the mild case is suggested by the fact that, regardless of the severity of the disease, that is, whether the cases did or did not require insulin, the degree of control of the diabetes, judging from the Control Index,[9] was better in the cases without than in those with arteriosclerosis. This, it may be noted, fits in also with the experiences of Richardson and his associates; the severity of the diabetes did not affect the incidence of arteriosclerosis in their group of cases.[11]

PLASMA CHOLESTEROL

In the study of the above-mentioned first group of 50 cases,[9] consideration was given to the metabolism of cholesterol as a possible factor. Since Aschoff first drew attention to the high cholesterol content in atheromatous aortæ in 1906 and Anitschkow first produced cholesterol atherosclerosis in the rabbit in 1913, much evidence had accumulated which supported the view that the high incidence of arteriosclerosis in diabetics was due to the high cholesterol content of the blood plasma, which is a characteristic of this disease. In the study of the above-mentioned group of 50 diabetics, particular attention was, therefore, paid to the plasma cholesterol values, and the data clearly showed that the average value was definitely higher in the arteriosclerotic than in the non-arteriosclerotic group. That the difference noted was not accidental, but causal, was shown by the ratio of the difference to its probable error. It was, therefore, suggested that the reduced incidence of premature arteriosclerosis noted was due to the marked reduction of the cholesterol content of the blood plasma, characteristic of the high carbohydrate-low calorie diet.[12, 13] It is to be noted here that, prior to this diet, though treatment resulted in a reduction of the cholesterol content of the blood plasma, as a rule, the average values were not as low as those obtained with the diets of higher carbohydrate and lower fat contents than those previously employed.[14] The intimate relationship between cholesterol metabolism and arteriosclerosis in diabetes has since then been stressed by a number of authors. For example, to the case of coronary thrombosis in a young diabetic reported by Cullinan and Graham,[15] and referred to then, may now be added that described by Reitman, Greenwood and Kler[16] and, perhaps, one of the most striking examples is the case of diabetes with marked hypercholesterolæmia and signs simulating cerebral thrombosis reported by the writer.[17] In support of the cholesterol theory there are also the comparative analyses of the lipids in the blood and atheromatous aortæ which suggest that the plasma is the source of the lipids deposited in the intima;[18] additional experimental cholesterol atheromatosis in another omnivorous animal,[19] and also the recent observations on the mechanism of lipophage deposition in atherosclerosis,[20] supporting Leary's

theory that atherosclerosis is caused by circulating lipophages.

PROTEIN METABOLISM

In the report of the above-mentioned second group of 50 cases,[5] improved protein metabolism was suggested as a possible factor in the postponement of the arteriosclerosis noted. It appeared reasonable that the greater the tendency towards a negative nitrogen balance, the more defective will be the nutrition and, therefore, the lower will be the resistance of the body to degenerative changes. Attention was, therefore, drawn to the fact that one of the striking characteristics of the high carbohydrate-low calorie diet was nitrogen retention.[21] As far as could be ascertained, the lowest urinary nitrogen excretions ever noted in man were noted with this diet.[12]

That duration of the diabetes, control of the diabetes, excess cholesterol in the blood and defective protein metabolism do not alone however explain the high incidence of arteriosclerosis in diabetes, seems clear from the still high incidence, in spite of the above-mentioned improvements in treatment. It is to be noted that, among the 50 cases in the 15-year group, 19 only had escaped this complication. The purpose here, therefore, is to present data which suggest another possible factor, namely, impairment of the detoxifying function of the liver.

THE LIVER IN DIABETES

It is of interest here to note that one of the oldest references to the pathology of diabetes pointed to the liver. Mead[22] first drew attention to the fatty infiltration in 1784. Fatty infiltration of the liver is a common post-mortem finding in deaths due to diabetic coma; it is readily produced in the depancreatized animal, and, as Best and his associates have shown, the condition is greatly exaggerated in spite of insulin therapy when the choline content of the diet is kept low.[23, 24] Enlargement of the liver is common in uncontrolled diabetes[25] particularly in children. Priscilla White[26] found palpable livers in 40% of her cases. In one case, the enlargement was such that the lower border was found in the pelvis.[27] A striking case of fluctuation of the size of the liver with the degree of control of the diabetes was reported by the writer,[28] and a somewhat similar case was met with recently in a child 8½ years old.

In addition to the above-mentioned anatomical changes, there is much evidence of functional disturbance also. In 1926, I[29] drew attention to the high incidence of excess quantities of bilirubin in the blood of diabetics. Of a group of 130 diabetics, selected at random, excess quantities of bilirubin were found in the blood in 34, an incidence of 26.1%. A high incidence was found in 1936 in a much larger group of cases and by a more exact method[28] and, in the same year, the writer showed that excess urobilinogen in the urine is also common in diabetics. Among 3,000 urine tests, excess quantities of urobilinogen were found in 822, an incidence of 27.4%.[30]

THEORY

Anatomically, the liver is interposed between the gastro-intestinal tract and the general circulation, and one of its important functions here is to detoxify harmful substances which reach it by way of the portal system and thus prevent their entry into the general circulation. Depending upon the nature of the substance that requires detoxification, the latter is accomplished by oxidation, reduction, conjugation, etc. A possibility which, therefore, has to be considered in the production of premature arteriosclerosis in diabetes is that, in the absence of a normally functioning liver, products of putrefaction in the intestinal tract which would otherwise be detoxified and thus not reach the general circulation, enter the latter and thus damage the tissues of the body, including the heart, arteries and kidneys.

When informed of this view and the proposed investigation to test it, Best's* observations, from his wide experience with liver changes in experimental diabetes, were as follows:

> "The more I think about it the more real seems to be the possibility of some interference with liver function under present conditions of diabetic treatment. Even with the best methods we have available for the administration of insulin, the control of liver function is by no means as adequate as under physiological conditions."

As far as is known, the detoxifying function of the liver and the part that this organ plays in the metabolism of bile pigments are independent of each other. It is also a well-known fact that the liver may fail in one of its functions and still function normally otherwise. The finding, therefore, of an excess of bilirubin in

* C. H. Best: Personal communication October 4, 1946.

the blood or of urobilinogen in the urine, does not necessarily imply failure of the detoxifying function.

SUGGESTIVE RELATIONSHIP BETWEEN LIVER FUNCTION AND PREMATURE DEVELOPMENT OF ARTERIOSCLEROSIS

The first suggestion of a possible relationship between liver function and premature development of arteriosclerosis was the improvement noted in the bilirubin content of the blood in relationship to diet and the relationship between the latter and the reduced incidence of arteriosclerosis during the same period. Since the above-mentioned high incidence of hyperbilirubinæmia was noted in 1926, determination of the bilirubin content of the blood has been a routine in practically every one of my cases. Since 1936, when the high incidence of excess urobilinogen in the urine was noted, this test has also been part of the routine. Many thousands of tests have thus been made and thus a sufficiently large number to be of statistical significance. In Table III are, briefly, summarized the experiences with over 5,000 van den Bergh tests selected at random in relationship to the various diets employed during that period.

It will be noted that, following the change of diet from the low carbohydrate-high fat to the high carbohydrate-low calorie[31] the incidence of hyperbilirubinæmia was reduced from 26.1 to 14.8%. Following the introduction of between-meal feedings of 10 gm. of carbohydrate, there was a still further reduction and, by increasing the amount of carbohydrate of the between-meal feedings to 20 gm., the incidence of hyperbilirubinæmia was reduced to its lowest level. It is also to be noted here that the changes of diet included protein; whereas, the low carbohydrate-high fat diets contained about 50 gm. of protein only, the first high carbohydrate-low calorie diet contained about 75 gm. The last modification contained 100 to 125 gm.[21]

Though, in all groups, the vast majority of tests were performed in cases under treatment, in each group there were tests on patients who had been seen for the first time. The extent to which liver function has been improved with this diet, at least insofar as the metabolism of bile pigments is concerned is, therefore, best seen in the last group of tests, in which those which had been made on patients under treatment were separated from those of patients seen for the first time. It will be noted that 3.1% only of the tests among the treated cases indicated bilirubin values greater than 1 unit (0.4 mgm.).

TABLE III.
RELATIONSHIP BETWEEN DIET AND INCIDENCE OF HYPERBILIRUBINÆMIA

Period	*Number of tests*	*Hyperbilirubinæmia**		*Diet*
		No.	*%*	
1926	130	34	26.1	Low carbohydrate-high fat**
1935	500	74	14.8	First high carboydrate-low calorie*†
1936	3000	232	7.7	First modification of high carbohydrate-low calorie (between-meal feedings of 10 gm. carbohydrate)†
1944: Total	2226	156	7.0	Second modification of high carbohydrate-low calorie (between-meal feedings of 20 gm. carbohydrate)††
New	692	108	15.6	
Old	1534	48	3.1	

*Bilirubin content of blood plasma—1 unit (0.4 mgm. per 100 c.c.) or more.
***Brit. J. Exp. Path.*, **7**: 155, 1926.
*†*Canad. M. Ass. J.*, **34**: 637, 1936.
†*Brit. J. Exp. Path.*, **17**: 249, 1936.
††Unpublished data since January, 1944.

The combined data, thus, fit in with the known damaging effects of low protein diets on liver function[32, 33, 34] and the beneficial effects of the high carbohydrate-low calorie diet, not only because of its high protein content, but because of the high biological value of the protein and the other conditions which tend towards storage of protein, namely, (*a*) the high carbohydrate content; (*b*) the low fat content, and (*c*) the between-meal feedings of carbohydrate. It is to be noted that the metabolism of tissue protein is never in abeyance.[35] Even under conditions of nitrogen equilibrium, endogenous (tissue) protein has been found to account for more than half of the total urinary nitrogen.[36] There is

also the fact that carbohydrates exert their maximum protein-sparing action only when they are available at the time when the intensity of protein metabolism is at its maximum[37] and, thus, whether nitrogen balance is or is not positive or negative depends upon the number of meals per day.[38]

EXPERIMENTAL

(*a*) *Relationship between urine urobilinogen and presence or absence of arteriosclerosis.*—Compared with the bilirubin content of the blood (van den Bergh reaction), the urobilinogen content of the urine, judging from the Wallace and Diamond test,[39] is a more sensitive test of impairment of liver function, insofar as bile pigment metabolism is concerned.*[40]

In view of the above experiences, therefore, as a preliminary step, it was considered of interest to compare the findings of 500 urobilinogen tests, selected at random, in cases of premature arteriosclerosis with a similar number of tests, selected at random, in cases with no detectable signs of this complication of diabetes. On the assumption that, with few exceptions, quantities of urobilinogen in excess of those detectable in dilutions greater than 1 in 20 were abnormal, the results of this study suggested that liver function and premature development of arteriosclerosis were related. Thus:

Group	*Number of cases*	*Excess urobilinogen* *Number*	*Percentage*
Arteriosclerosis	500	239	47.8
No arteriosclerosis	500	148	29.6

(*b*) *Relationship between degree of control of diabetes and excretion of urobilinogen in urine.*—Poor control of the diabetes tends to produce enlargement and fatty infiltration of the liver. Therefore, provided impairment of function paralleled the degree of fatty infiltration, larger excretions of urobilinogen would be expected when the diabetes is under poor control than when under good control. To determine the extent to which excretion of urobilinogen parallels the control of the diabetes, 200 tests were selected at random from the records and, in each case, the urobilinogen excretion was correlated with the Control Index. The data are briefly summarized in Table IV. It will be noted that, statistically, a definite relationship was found between the degree of control of the diabetes and degree of impairment of liver function, at least insofar as the metabolism of this bile pigment is concerned. The parallelism is still more marked when consideration is given to the relatively small number of observations and the frequency of wide fluctuation both in the blood sugar and urobilinogen contents of the urine even in moderately severe diabetes.

TABLE IV.

RELATIONSHIP BETWEEN UROBILINOGEN CONTENT OF URINE AND DEGREE OF CONTROL OF DIABETES (CONTROL INDEX)

*Urobilinogen**	*No.*	*Control index***				
		0	1	2	3	M†
1: 10	82	0	13	45	24	2.13
1: 20	41	0	5	22	14	2.22
1: 50	17	0	2	7	8	2.35
1: 100	21	1	7	8	5	1.81
1: 250	15	1	7	5	2	1.53
1: 500	11	0	5	4	2	1.73
1: 1000	6	0	4	2	0	1.33
1: 1000+	7	0	5	2	0	1.29

*Figures denote maximum dilution of urine in which urobilinogen was noted.

For calculation of Control Index, see *Ann. Int. Med.*, **8: 1436, 1935.

†M = Average

Briefly, therefore, at this stage of the investigation it was clear that poor control of the diabetes causes derangement of the liver not only organically (enlargement and fatty infiltration) but also functionally, at least insofar as the metabolism of bile pigments is concerned. Whether the detoxifying capacity of the liver is also impaired was not known. The next step, therefore, was to employ various tests of detoxifying capacity—thymol, glycuronic test, indican reaction, hippuric acid test, etc.—and, briefly, none was found satisfactory. This, however, it should be noted, is not in accordance with experiences of others.[42, 43]

* Notwithstanding Watson's more quantitative method of estimating urobilinogen,[41] the Wallace and Diamond procedure[39] slightly modified[40] was selected for this study, because of its simplicity and also because the earliest effect of impaired liver function is periodic excretion of excess quantities, the total amount of urobilinogen in 24 hours still being within the upper limit of normality, namely, 4 mgm. per 24 hours. Experience with many thousands of these tests has, however, shown that the most reliable results are obtained with chance samples, only when the test is performed on urine immediately after the sample is obtained, for not only does the temperature of the reacting mixture influence very greatly the intensity of the colour formation, but any delay in the performance of the test reduces the amount of urobilinogen present and, thus, further decreases the colour formation. Diuresis must also be avoided, since dilution of the urine also influences the intensity of the colour. High values are particularly significant, since, normally, the smallest and most constant excretions of urobilinogen occur in the morning.[40]

(c) *Relationship between control of diabetes, reaction to ingestion of indole and excretion of urobilinogen in urine.*—A clinical test of detoxifying capacity of the liver which I have used for some time, though now rarely mentioned in the literature, is the response to ingestion of indole.[44] Normally, some of the indole is detoxified by bacterial action in the intestinal tract, but that the liver plays an appreciable part is suggested from the effects of its ingestion in disease of the liver. Normally, ingestion of 50 mgm. appears to be harmless. When, however, it is not detoxified properly, it causes foul breath, loss of appetite, distinct nausea, belching and, in some cases, severe headache which may persist for 12 hours or more. Vomiting is rare. In earlier studies, an attempt was made to employ the urinary excretion of indole as a test of detoxifying capacity; but as the amounts found showed little or no relationship to the clinical signs and symptoms of intoxication, this laboratory test was also discarded. The indole is administered in a capsule, coated so that it will pass through the stomach into the intestines unaltered.

TABLE V.

RELATIONSHIP BETWEEN DEGREE OF CONTROL OF DIABETES (CONTROL INDEX) AND UROBILINOGEN CONTENTS OF URINE IN CASES WITH AND WITHOUT INDOLE REACTIONS

*Urobilinogen**	*No.*	*No indole reactions*				
		*Control index***				
		0	1	2	3	M†
1: 10	60	0	7	35	18	2.18
1: 20	21	0	2	8	11	2.43
1: 50	6	0	1	2	3	2.33
1: 100	3	0	0	2	1	2.33
1: 250	4	0	1	2	1	2.00
1: 500	2	0	0	2	0	2.00
1: 1000	3	0	2	1	0	1.33
1: 1000+	1	0	1	0	0	1.00

*Urobilinogen**	*No.*	*Indole reactions*				
		Control index				
		0	1	2	3	M
1: 10	22	0	6	10	6	2.00
1: 20	20	0	3	14	3	2.00
1: 50	11	0	1	5	5	2.36
1: 100	18	1	7	6	4	1.72
1: 250	11	1	6	3	1	1.36
1: 500	9	0	5	2	2	1.66
1: 1000	3	0	2	1	0	1.33
1: 1000+	6	0	4	2	0	1.33

*Figures denote maximum dilution of urine in which urobilinogen was noted.

**For calculation of Control Index, see *Ann. Int. Med.*, 8: 1436, 1935.

†M = Average

To determine the extent to which, if any, response to ingestion of indole parallels the excretion of urobilinogen, comparative tests were made until 100 individuals were collected who responded abnormally to the ingestion of the indole, according to any one of the above-mentioned signs of intoxication, and these were compared with 100 cases selected at random from the far greater number who had reacted normally. In each case, also, was calculated the Control Index. The combined data are briefly summarized in Table V.

Here, it will be noted that, though the correlation between the degree of control of the diabetes and excretion of urobilinogen was not as close as in Table IV, the largest excretions of urobilinogen were associated with the poorest controls of the diabetes. The correlation was closer in those who had reacted abnormally to the ingested indole than in those who showed no signs of intoxication. It will also be noted that the incidence of large excretions of urobilinogen was greater among the cases that manifested toxic signs than among those who reacted normally. Thus, though bile pigment metabolism and detoxification are probably independent functions of the liver, and though, as in the case of the other functions, one may be impaired without impairment of the other, there is some evidence that, when there is impairment of bile pigment metabolism, there is also some liver failure of detoxifying capacity.

RELATIONSHIP BETWEEN CONTROL OF DIABETES, REACTION TO INDOLE, EXCRETION OF UROBILINOGEN AND PRESENCE OR ABSENCE OF ARTERIOSCLEROSIS

In view of the above findings, indole was administered to diabetics with premature arteriosclerosis (under age 50 years) until there were 50 cases with toxic signs. In each case, immediately before the indole was given, a fresh specimen of urine was subjected to the urobilinogen test, as well as for sugar, acetone, etc., and a sample of blood was obtained for the Control Index. The data so obtained were then compared with an equal number of individuals who had been subjected to the same tests under the same conditions, but who had no detectable signs

of premature arteriosclerosis. The combined data are, briefly, summarized in Table VI. The following points are to be noted:

Compared with the previously noted relationship between control of the diabetes and excretion of urobilinogen (see Table IV) the findings

TABLE VI.

RELATIONSHIP BETWEEN DEGREE OF CONTROL OF DIABETES (CONTROL INDEX) AND UROBILINOGEN CONTENT OF URINE IN CASES WITH AND WITHOUT INDOLE REACTIONS AND WITH AND WITHOUT ARTERIOSCLEROSIS.

*Urobilinogen**	ARTERIOSCLEROSIS												
	No.	*Indole reactions*						*No indole reactions*					
		*Control index***						*Control index*					
		No.	0	1	2	3	M†	*No.*	0	1	2	3	M
1: 10	9	5	0	1	2	2	2.20	4	0	0	2	2	2.50
1: 20	5	3	0	1	2	0	1.66	2	0	1	1	0	1.50
1: 50	12	5	1	2	2	0	1.20	7	0	2	4	1	1.86
1: 100	7	4	0	1	2	1	2.00	3	0	0	1	2	2.66
1: 250	5	2	1	0	1	0	1.00	3	0	1	0	2	2.33
1: 500	8	6	1	3	1	1	1.33	2	0	1	0	1	2.00
1: 1000	2	2	0	1	1	0	1.50	0	0	0	0	0	.....
1: 1000+	2	1	0	1	0	0	1.00	1	0	0	1	0	2.00

*Urobilinogen**	NO ARTERIOSCLEROSIS												
	No.	*Indole reactions*						*No indole reactions*					
		Control index						*Control index*					
		No.	0	1	2	3	M	*No.*	0	1	2	3	M
1: 10	15	6	0	2	1	3	2.17	9	0	3	2	4	2.11
1: 20	4	1	0	0	1	0	2.00	3	0	0	2	1	2.33
1: 50	13	4	0	1	1	2	2.25	9	0	3	1	5	2.22
1: 100	5	4	0	1	3	0	1.75	1	0	0	1	0	2.00
1: 250	6	1	0	0	1	0	2.00	5	0	1	3	1	2.00
1: 500	4	0	0	0	0	0	.....	4	0	1	1	2	2.25
1: 1000	2	2	0	1	1	0	1.50	0	0	0	0	0	.....
1: 1000+	1	0	0	0	0	0	.....	1	0	0	0	1	3.00

*Figures denote maximum dilution of urine in which urobilinogen was noted.
For calculation of Control Index, see *Ann. Int. Med.*, **8: 1436, 1935.
†M = Average

In general, the control of the diabetes was better in the non-arteriosclerotic than in the arteriosclerotic group. The higher incidence of large excretions of urobilinogen (pigment detected in dilutions of 1 in 250 or more) occurred in the arteriosclerotic group. Among the 50 individuals in the latter group, such excretions were found in 17, an incidence of 34%; whereas, of the 50 cases without arteriosclerosis, there were 13 such excretions only, an incidence of 26%. Toxic signs from the ingested indole were noted in 28 of the 50 cases with arteriosclerosis, an incidence of 56%; whereas, in the 50 cases with no detectable arteriosclerosis, there were 18 only, an incidence of 36%.

in this group of cases were more irregular. The correlation between the degree of control of the diabetes and the excretion of urobilinogen was closest in the individuals with arteriosclerosis who showed toxic signs from the ingested indole.

DISCUSSION

A relationship was noted between the degree of control of the diabetes, excretion of excess quantities of urobilinogen in the urine, toxic reactions to indole and the presence or absence of premature arteriosclerosis. In all, though no definite proof was found, the data are consistent with the view that impairment of the detoxifying capacity of the liver is a factor in the premature development of arteriosclerosis in

diabetes mellitus; that in the absence of a normally functioning liver, products of intestinal putrefaction, which would otherwise be detoxified, reach the general circulation, damage the tissues and thus tend towards the development of arteriosclerosis prematurely.

The findings are not inconsistent with the view that excess cholesterol in the blood is a factor. It is possible that the same cholesterol which is eventually deposited in the blood vessels also damages the liver. As previously suggested by the writer[28] constant exposure to excess quantities of cholesterol in the blood might have the same effects upon the liver in the human being as those which were found by Best and his co-workers in animals after feeding cholesterol. Dr. J. E. Pritchard, pathologist at the Montreal General Hospital, has been impressed for some time with the uncommon finding of fatty livers at autopsies of diabetics, compared with frequency prior to the use of the high carbohydrate-low calorie diet. These experiences fit in with previously reported finding that the high carbohydrate-low calorie diet was more effective in controlling the diabetes than all other methods of treatment reported before then.[45] Of interest here is the report of a case of typhoid fever in a child 8 years with marked enlargement of the liver due to excess cholesterol esters.[46]

The findings are also not inconsistent with the previous suggestion that defective protein metabolism may be a factor in the premature development of arteriosclerosis, since both normal liver function and resistance to nutritional disturbances require an adequate intake of protein and under conditions which tend towards nitrogen equilibrium and storage, rather than towards a negative balance. The number of cases investigated was, however, small. The purpose of this report was merely to report the findings to-date so that others with similarly available clinical and laboratory facilities may add their experiences.

REFERENCES

1. ROOT, H. F., BLAND, E. F., GORDON, W. H. AND WHITE, P. D.: *J. Am. M. Ass.*, 113: 27, 1939.
2. LISA, J. R., MAGIDAY, M., GALLOWAY, I. AND HART, J. F.: *J. Am. M. Ass.*, 120: 192, 1942.
3. JOSLIN, E. P. *et al.*: Treatment of Diabetes Mellitus, Lea & Febiger, Philadelphia, 6th ed., 1937.
4. WARREN, S.: The Pathology of Diabetes Mellitus, Lea & Febiger, Philadelphia, 2nd ed., 1938.
5. RABINOWITCH, I. M.: *Canad. M. A. J.*, 51: 300, 1944.
6. JOSLIN, E. P. *et al.*: Treatment of Diabetes Mellitus, Lea & Febiger, Philadelphia, 7th ed., 1940.
7. DOLGER, H.: *J. Am. M. Ass.*, 134: 1289, 1947.
8. WARREN, S.: The Pathology of Diabetes Mellitus, Lea & Febiger, Philadelphia, 1930.
9. RABINOWITCH, I. M.: *Ann. Int. Med.*, 8: 1436, 1935.
10. RABINOWITCH, I. M., RITCHIE, W. L. AND MCKEE, S. H.: *Ann. Int. Med.*, 7: 1478, 1934.
11. RICHARDSON, R., BOWIE, M. A., EDEIKEN, J., LEOPOLD, I. H. AND NAIDE, M.: *Am. J. M. Sc.*, 209: 1, 1945.
12. RABINOWITCH, I. M.: *New Eng. J. Med.*, 204: 799, 1931.
13. *Idem*: *Canad. M. A. J.*, 28: 162, 1933.
14. *Idem*: *Canad. M. A. J.*, 17: 171, 1927.
15. CULLINAN, E. R. AND GRAHAM, F.: *J. Path. & Bact.*, 36: 167, 1934.
16. REITMAN, N., GREENWOOD, W. R. AND KLER, J. H.: *Am. J. M. Sc.*, 203: 792, 1942.
17. RABINOWITCH, I. M.: *Canad. M. A. J.*, 40: 257, 1939.
18. MCARTHUR, C. S.: *Bioch. J.*, 36: 559, 1942.
19. DAUBER, D. V. AND KATZ, L. N.: *Arch. Path.*, 34: 937, 1942.
20. GORDON, I.: *Arch. Path.*, 44: 247, 1947.
21. LOVELL, M. E. AND RABINOWITCH, I. M.: *J. Nutrit.*, 18: 1339, 1939.
22. MEAD, R.: Cited by Shields Warren, see Ref. 8.
23. BEST, C. H., FERGUSON, G. C. AND HERSHEY, J. M.: *J. Physiol.*, 79: 94, 1933.
24. BEST, C. H. AND CHANNON, H. J.: *Bioch. J.*, 29: 2651, 1935.
25. HANSSEN, P.: *J. Am. M. Ass.*, 106: 914, 1936.
26. WHITE, P.: Quoted by Joslin, E. P., *New Eng. J. Med.*, 209: 519, 1933.
27. WHITE, P.: Diabetes in Childhood, Lea & Febiger, Philadelphia, 1932.
28. RABINOWITCH, I. M.: *Canad. M. A. J.*, 34: 637, 1936.
29. *Idem*: *Brit. J. Exp. Path.*, 7: 155, 1926.
30. *Idem*: *Brit. J. Exp. Path.*, 17: 249, 1936.
31. *Idem*: *Canad. M. A. J.*, 23: 489, 1930.
32. MILLER, L. L. AND WHIPPLE, G. H.: *Am. J. M. Sc.*, 199: 204, 1940.
33. HIMSWORTH, H. P. AND GLYNN, L. E.: *The Lancet*, 1: 457, 1944.
34. KOSTERLITZ, H. W.: Proc. Bioch. Soc., *Biol. J.*, 38: No. 3, xv, 1944.
35. BORSOOK, H. AND KEIGHLEY, G. L.: *Proc. Roy. Soc.*, 118: 488, 1935.
36. BEARD, H. H.: *Human Biology*, 1: 419, 1935.
37. LARSON, P. S. AND CHAIKOFF, I. L.: *J. Nutrit.*, 13: 287, 1937.
38. CUTHBERTSON, D. P. AND MUNRO, H. N.: *Bioch. J.*, 33: 488, 1939.
39. WALLACE, G. B. AND DIAMOND, J. S.: *Arch. Int. Med.*, 35: 698, 1925.
40. RABINOWITCH, I. M.: *Canad. M. A. J.*, 25: 255, 1931.
41. WATSON, C. J.: *Arch. Int. Med.*, 59: 196, 206, 1937.
42. MATEER, J. G. *et al.*: *Gastroenterology*, 8: 52, 1947.
43. *Idem*: *J. Am. M. Ass.*, 133: 909, 1947.
44. NOVELLO, N. J., WOLF, W. AND SHERWIN, C. P.: *Am. J. M. Sc.*, 170: 888, 1925.
45. RABINOWITCH, I. M.: *Canad. M. A. J.*, 33: 136, 1935.
46. BEUMER, H.: *Jahrb. f. Kinder*, 145: 265, 1935.

1020 Medical Arts Bldg.

NUTRITION IN PREGNANCY*

Henri Simonnet, M.D.†

Paris, France

IN 1942, Ebbs, Scott and co-workers, in a paper published in *The Canadian Medical Association Journal*[1] reported the results of an exhaustive study of the effects of diets classed as poor, good, and supplemented, on 400 expectant mothers. Some of their observations were as follows:

"The rôle of nutrition in the growth and development of the infant has been recognized for a long time, but the relation of adequate diet for the mother during pregnancy to fetal mortality rates has not been recognized. . . . The inereased demands upon the maternal organism during pregnancy are well recognized. . . . If the mother's diet is only barely adequate for her own needs, the increasing demands of the parasitic fetus will make the diet deficient for the mother. If the diet is already inadequate, the deficiencies will become even greater if the needs of the fetus are satisfied." They further add,

* The lecture on "Nutrition in Pregnancy" was given at McGill University, Wednesday, December 17, 1947.

† Guest Professor, University of Montreal, September-December, 1947.

"The application of the principles of nutrition could not be more important in any other period of life than during pregnancy."

On the other hand, R. Garry and H. Wood in a good review on dietary requirements in human pregnancy and lactation,[2] write:

"During the ten years which have elapsed since our last review of 1936, on the dietary requirements during pregnancy and lactation, it is surprising that few fundamental additions have been made to our scientific knowledge on the subject."

A more skeptical attitude has developed amongst biologists and they have become more humble relative to their ignorance of the relations between nutrition, pregnancy and lactation.

It is important to recall briefly the means of investigations we have to study the relations between nutrition and pregnancy. Physiology and pathology give us important guidance, but they are not sufficient. It is indeed difficult to study an organism as well protected against our curiosity as the embryo of the mammals. On the other hand, it is difficult and even unsafe to extrapolate from one species of mammals to another, due to the very noticeable differences in the structure of the placenta. *A fortiori* the study of the embryonal development of the bird, so easy to follow, has indeed very little interest in the present case.

Apart from these data, a study of the relations between nutrition and pregnancy must be supported by what is revealed by the following three methods: (1) Surveys on spontaneous nutrition during pregnancy. (2) Theoretical data concerning substances necessary to the development of the ovum, fetus, membranes, amniotic fluid, also uterine and mammary developments. These data represent a minimum, the value of which must be multiplied by a coefficient depending: (*a*) on the availability of the nutriments for the pregnant woman; (*b*) on their availability for the fetus. The proposed nutritive standards, evidently temporary, are nevertheless interesting. Their comparison with the consumption of an individual, or of a group of individuals, may well enable us to trace some deficiencies and may permit an improvement in nutrition. (3) On the other hand, wherever deficiencies are found, the appreciation of a state of health or of sickness, with the mother, as well as with the fetus or the newborn, will allow useful conclusions concerning the value of standards, the importance, significance and seriousness of the revealed deficiencies.

All these studies have led to known standards of nutrition which were proposed in 1945 by the Food and Nutrition Board of the National Research Council of Washington, replacing those of 1943. They are generally adopted by all countries participating in the F.A.O., Food and Agriculture Organization of the United Nations.

TABLE I.

RECOMMENDED DIETARY ALLOWANCES (REVISED 1945)
(National Research Council) Washington
Amounts per day—Woman 123 lb. (56 kg.)

	Not pregnant		*Latter half of pregnancy*
	Sedentary	*moderately active*	*(sedentary)*
Calories	2,100	2,500	2,500[1]
Protein gm.	60	60	85
Calcium gm.	0.8	0.8	1.5
Iron mgm.	12.0	12.0	15.0
Vitamin A U.I.	5,000	5,000	6,000
Thiamine mgm.	1.1	1.2	1.8
Riboflavin mgm.	1.5	1.6	2.5

These nutrition standards afford a good margin of safety, they take into account the losses due to the preparation of food, losses due to paring, cooking and consumption. They do not take into account all nutrition needs, chiefly those concerning trace elements, nor certain vitamins, the need of which is not yet definitely established. Until proof to the contrary, one believes that these substances are automatically furnished by a good mixed diet.

These standards should be expressed in the form of appropriate food and diets, based on the financial means and physical condition of each individual. And this is not the easiest problem to solve.

Of all nutritive needs, chemical energy in the form of carbohydrates, fats and protein, is the most important, on account of its volume. Also because of the various fundamental functions which changes of energy play in the maintenance of life. In spite of what might be expected, the basal metabolism does not increase during pregnancy. But total metabolism is definitely increased from 10 to 12%, from the twelfth week on. This increase is evidently due: (*a*) to the energy spent in the building of new tissues; (*b*) to the additional mechanical work brought to the mother on account of her increased weight; (*c*) to the supplementary labour of the heart related to the fetal circulation.

The problem of direct stimulation of thyroid function remains unsolved. We must not forget that during pregnancy, the hypophysis undergoes structural and functional alterations, the

repercussions of which on its metabolic functions are still to be understood.

We only possess partial information concerning the particular needs in carbohydrates and fats. Let us recall that during the latter weeks of pregnancy, a marked tendency to hypoglycæmia is noted, accompanied by an increase in tolerance to carbohydrates and a remarkable inclination to ketosis. A preventive action as regards toxæmia in pregnancy is afforded by a liberal supply of sugar, in any case, it results in a protection for the hepatic cells.

With reference to fats, one might think that the alimentary supply of lipoids must be considered, in relation to the high quantity of progesterone and œstrogens which are produced during pregnency.

PROTEIN REQUIREMENTS

Our attention has been specially attracted by the problem of protein requirements. It is generally admitted that the protein needs during pregnancy are especially high. As a matter of fact, this increase is not so high if we consider the nitrogen fixation produced during pregnancy.

TABLE II.

Lunar month	*Total weight of the ovum gm.*	*Protein gm.*
2	17.0	0.0
3	32.0	0.625
4	118.0	3.375
5	304.0	20.0
6	606.0	50.0
7	1026.0	101.0
8	1255.0	135.0
9	1710.0	234.0
10	3535.0	454.0

The increase is therefore noticeable only from the beginning of the second half of pregnancy.

Ignorant as we are of the biological value of alimentary proteins for the fetus and of its needs in essential amino-acids, we must adopt the same values as during growth. The value of 1.5 gr. daily per kg. is adopted as a basis provided at least 50% of the protein is of animal origin. One must remember that during pregnancy, large retentions of nitrogen are made by the maternal organism in excess of the requirements of the fetus. Let us note also that the fetal blood contains a higher proportion of amino acids than the maternal blood: 8.1 mgm. per 100 as against 6.9 mgm. per 100.

We must also insist upon the necessity of systemic biochemical studies establishing comparison between mother and fetus. These studies afford a better understanding of the transfer between the two organisms, and render the fetal metabolism more comprehensible. Whether a diet rich in proteins is favourable to the accidents of toxæmia in pregnancy, remains an unsolved problem. Homes[3] reports that toxæmia is more frequent with values of 1 gm. than with 2 gm. or more.

Water metabolism offers some interest during pregnancy. In the first place, it is closely related to the metabolism of sodium chloride, from which it cannot be separated, and then it is also related to the protein metabolism. It is directly or indirectly associated with toxæmia accidents by accumulation of extracellular fluids. Under normal conditions, if the intake of sodium chloride is not controlled, a weekly retention from 200 gm. to 300 gm. water is noted during the last two months of pregnancy.

MINERALS

When fully developed, the fetus has accumulated in its tissues, calcium 25 gm.; phosphorus 14 gm.; magnesium 0.600; iron 0.400.

These are important quantities, even if not very high, as compared with maternal reserves. In case of deficiency, the mother must always compensate; the fetus depends on her for its security. Her bone structure loses its calcium and exposes her to osteomalacia, her iron reserves are depleted at the expense of the building of her red cells. The fetus will thus acquire its sufficient iron hepatic reserve which will allow it to overcome the deficiency of iron in milk.

Calcium.—The requirements of calcium have been set at 1.5 mgm. daily by the National Research Council of Washington. The figure is rather high and implies a large consumption of milk products or their derivatives, and often calcium salts in their natural state. In the latter case, the problem of availability and intestinal resorption of various types of alimentary calcium arises. When calcium supplies are sufficient, there is no danger of any deficiency in phosphorus. The equilibrium between Ca and P must always be controlled and remain around the figure one to insure proper assimilation of these two elements.

Iron.—The allowance of iron has been set at 15 mgm. daily. This figure is high enough to insure a good safety margin. But one must consider the resorption of alimentary iron which is not always present under an appropriate form. The possibility of maternal anæmia due to deficiency of alimentary iron has been well established in Great Britain during the last war, and has been confirmed in France during the years of occupation. The use of radio-active iron has shown that a pregnant woman resorbs from two to ten times more iron than the normal woman.

Iodine.—The increased needs for iodine during pregnancy are beyond doubt. Here are some proofs: (1) The iodine content of the blood is doubled during pregnancy. (2) The administration of iodized salt reduces considerably the weight of the thyroid of the newborn in goitre countries such as Switzerland in the state of Bern. During 1924, before iodized salt was used, the mean weight of the thyroid was 8.87 gm., during 1929, 6.99 gm. and in 1936, iodized salt having been generally used, 3.70 gm. (3) General use of iodine reduces idiopathic stillbirth. The following data have been collected by Kemp:[4] (*a*) In the practices of physicians prescribing prenatal iodine routinely, deliveries 742; stillbirth 17 (2.29%); idiopathic stillbirth 1 (0.134%). (*b*) In the practices of physicians seldom or never prescribing prenatal iodine, deliveries 4,071; stillbirth 118 (2.9%); idiopathic stillbirth 49 (1.203%).

Trace elements.—Data on this point are rather scarce. The needs of manganese, zinc, cobalt and nickel are assured by a mixed diet. The same thing applies to copper; its importance as a hæmatopoietic agent is well known. The hepatic reserve to be formed by the fetus should be about 7 mgm.

Vitamins.—The vitamin problem during pregnancy does not differ essentially from the other problems created by other nutritive principles. However, it offers various aspects, whether we consider the consequences of the deficiency of a specific vitamin for the mother or the fetus, or the results achieved by the extensive use of such vitamins as therapeutic agents.

A comprehensive study of the question would also include: (1) The estimation of the vitamin needs during pregnancy, including the ability of the mother to build vitamin reserves. (2) The function of the placenta in transferring vitamins from mother to fetus. (3) The ability of the fetus to accumulate vitamin reserves. These will permit him to safely undertake the first months of his existence during which milk will be his sole food.

I shall make a few general remarks only. It is admitted that the needs for vitamins during pregnancy increase considerably. This increase corresponds, or rather is equivalent to the normal needs of a growing organism. All observation and experience is in direct support of this statement, such as signs of pre-deficiency with mothers; blood level of vitamins: urinary level with or without saturation. This increase is particularly noticeable in the case of vitamin A, thiamine and ascorbic acid. For instance, Toverud noted that 46% of a group of 114 pregnant women excreted practically no vitamin B-1, and 8 out of 10 none, after a test dose of 5 mgm.

Vitamin reserves are, by definition, always low. This explains why during pregnancy, it is always recommended to increase their intakes. Here again the mother acts as a safety factor and it seems that the requirements of the fetus are always fulfilled at the expense of the maternal organism. It is often said that the fetus behaves as a parasite in relation to his mother. This explains why it is advisable to improve the maternal alimentation during the first half of the pregnancy, although the needs of the fetus are very restricted during this period.

The rôle of the placenta.—The transfer of vitamin A to the fetus appears to be controlled by various factors which have not been fully investigated. The fetal blood vitamin A is often lower than the mother's, sometimes higher. The concentration of vitamin C in the blood plasma of the umbilical cord has been found by a number of investigators to be from 1.5 to 4 or more times that present in the maternal blood at the time of delivery.

For instance, in a group of 22 hospital cases, Braestrup,[5] obtained average values of 0.26 mgm. of vitamin C per 100 c.c. of maternal blood and 1.07 mgm. for the blood value of the umbilical cord. McDevitt and co-workers have presented proofs that the placenta exerts selective action in filtering vitamin C from the maternal blood.

Fetal reserves.—If maternal reserves are low, those of the fetus are not generally very important. Such is the case for vitamin A, B and especially K. The cases of hæmorrhagic disease in the newborn are often due to a dietary deficiency in vitamin K of the mother during pregnancy. This deficiency prevents the fetus from storing a sufficient reserve of the vitamin.

Anæmia.—Pregnancy is often associated with anæmia in the mother. Hæmo-dilution is largely responsible for this condition. Nevertheless, apart from iron deficiency, all other vitamin deficiencies of group B may be present. Amongst vitamins most indicated to improve this condition niacinamide and, chiefly, folic acid are most important.

The etiology and pathogenesis of hyperemesis gravidarum and of the toxæmia of pregnancy are not yet elucidated. It is therefore not surprising that various deficiencies have been blamed, for instance, deficiencies of vitamins B and C. It must be recognized, however that the use of vitamin B in the treatment of toxæmias of pregnancy has been disappointing. As the œdema that characterizes most of the toxæmias of the latter part of pregnancy has been ascribed in part at least to an increased capillary permeability, Shute has proposed the use of vitamin P in such a condition.

The need of vitamin D during pregnancy is a well established fact. McLennan suggests that mild osteomalacia may explain why some women who have had no difficulty in earlier labours may appear in later ones to have a slight contraction of the pelvis. Children of mothers deficient in vitamin D have been reported to have soft skulls, poorly calcified bones and to develop rickets easily or even to be born with rickets. But too much vitamin D may cause calcification of the fetal bones of the head, making birth difficult. During the German occupation obstetricians noticed in France that labour was easier owing to the elasticity of the poorly calcified bones of the newborn.

Much has been written on the prevention of recurrent abortion and threatened abortion by vitamin E. Therapeutic measures have not confirmed the experimental results obtained on laboratory animals. However, Winkler's report should be remembered, that 30 mgm. of alphatocopherol administered daily increases the low urinary excretion of pregnandiol which is observed in some cases of threatened abortion. This observation brings out the important and still unsettled problem of the relation between hormones and vitamins. Javert and Stander[6] believe that lack of vitamins C and K may be a factor in the pathogenesis of threatened and spontaneous abortion and antepartum bleeding.

Before concluding I should like to report amongst many interesting experiments, those of Kappeli[7] concerning the possible influence of vitamin C on uterine contraction. Kappeli states that in the isolated guinea-pig uterus, the addition of vitamin C to the perfusing liquid causes an increase of the uterine tone and reinforces the effect of pituitary extract. In large doses it produces a slow, steadily increasing uterine contraction which either becomes rhythmic or passes into tetany. The action on the human uterus is variable but vitamin C strengthens and prolongs the uterine contractions caused by pituitary extract.

Vitamin B_1 has been proposed as a means of accelerating labour. It induces also a slight anæsthesia in 40% of the cases.[8]

CONCLUSIONS

1. Nutrition must be considered as an entity. No particular constituent is more important than another. Each nutriment should be present in its optimum quantity. No better results would be achieved by increasing one at the expense of the other.

2. A proper adjustment of the expectant mother's food supply is useful and necessary, not only for the welfare of the fetus and mother, but also to provide for proper lactation.

3. Care should also be taken during the intervals between two pregnancies to allow the mother to recuperate from her previous stress.

4. Standards of nutrition are averages which should be adapted to each case according to the age, constitution, heredity and health condition of the mother.

5. The difficulty of the problem is the computing of a diet which agrees with the nutrition standards and permits the availability of the proper foods.

6. This requires close co-operation between physician, dietician and nurse, above all the complete assistance of the expectant mother

who should be informed of the main topics concerning her needs and those of her child.

REFERENCES
1. EBBS, J. H.; SCOTT, W. A. *et al.*: *Canad. M. A. J.*, 46: 1 and 6, 1942.
2. GARRY, R. C. AND STIVEN, D.: *Nutr. Abs. & Rev.*, 5: 855, 1936.
3. HOLMES: *Western J. Surg., Obst. & Gyn.*, 49: 56, 1941.
4. KEMP, W. N.: *Canad. M. A. J.*, 41: 356, 1939.
5. BRAESTRUP, P. W.: *J. Nutr.*, 16: 363, 1938.
6. JAVERT, C. T. AND STANDER, H. J.: *Surg., Gyn. & Obst.*, 76: 115, 1943.
7. KAPPELI, W.: *Helv. Med. Acta.*, 7: 169, 1940.
8. SCHUB, R.: Foreign Letters, *J. Am. M. Ass.*, 133: 122, 1947.

THE SURGICAL MANAGEMENT OF CHRONIC DUODENAL ULCER WITH SPECIAL REFERENCE TO THE ROLE OF VAGOTOMY*

P. H. T. Thorlakson, M.D.†

Winnipeg, Man.

THE medical and surgical management of duodenal ulcer has occupied an increasingly prominent place in medical discussion during the past fifty years. Prior to this period, the textbooks of the eighties and nineties contained little more than a reference to this common and important problem of today. Although the possibility of an increasing incidence of duodenal ulcer is not involved in this discussion, it is nevertheless true that patients are presenting themselves in increasing numbers with this disease. They are seeking relief not only from recurrent attacks of dyspepsia but too often because of intractable pain, hæmorrhage, perforation or obstruction which represent usually the late and advanced complications of this condition. The resultant misery and disability must interfere with the individual's pursuit of happiness and represent a serious economic problem. Moreover, the considerable discussions as well as the continuing large volume of research on the subject indicate that a wholly satisfactory solution to the problem of chronic duodenal ulcer is not yet available.

There is no doubt, and it is generally accepted, that the large proportion of cases of uncomplicated duodenal ulcer are well served by medical measures which are directed towards correcting the local and general factors commonly recognized to be of importance. On the other hand, a definite proportion of uncomplicated ulcers, approximately 10%, fail to be controlled, for various reasons, by medical means and require surgery. These cases are distinct from an equally definite group which, because of complications, demand surgery.

It may be said without equivocation that the surgeon who undertakes the treatment of complicated duodenal ulcer is dealing with one of the most difficult problems in medicine. This type of case represents a failure of medical therapy and a lesion which has become progressively worse as the years go by. The ulcer by this time has produced such an extreme technical problem that it must be dealt with radically if surgery is to succeed. At this juncture it is essential to emphasize, and without apology, to the internist and to the physician who may be apt to criticize the results of surgery in this group of cases, that such patients are suffering from more than a simple ulcer. The criteria of success cannot be comparable to those expected in the medical therapy of an uncomplicated and relatively superficial lesion. On the contrary, a whole procession of complex pathological processes combined with physiological and biochemical upsets has been set in motion. One has only to mention pyloric obstruction, local pancreatitis due to extension of the ulcer, which may interfere perhaps with biliary drainage and liver function, and the concomitant malnutrition and anæmia to realize what a challenge faces the surgeon in seeking a successful issue in some cases.

The great problem for all of us, whether he be physician or surgeon, is to recognize the proper time, insofar as it may be possible, when medical treatment should give way to surgery. This is frequently a difficult decision. I must confess that I have been responsible too often for insisting on further trial of medical treatment when, in retrospect, I realize that my judgment has been at fault. Out of this general conservative attitude have arisen some of the most difficult technical tasks I have encountered in the past fifteen or twenty years.

It has been the realization of the technical obstacles that confront the average surgeon in attempting to remove a deeply penetrating ulcer with its attendant œdema and inflammation of tissues, that has led me to take a special interest in the possibility of vagus resection and posterior gastro-enterostomy in the treatment of the

* A Founders' Lecture delivered at the Annual Meeting of the North Pacific Surgical Association in Victoria, British Columbia, November 21, 1947.

† Division of Surgery, Winnipeg Clinic.

advanced type of case. This is so, although I believe that, in the face of our present incomplete knowledge of the etiology of duodenal ulcer, a radical excision of the lower 70% of the stomach including the ulcer offers the patient the best assurance of relief from his symptoms and protection from anastomotic ulcer.

It is safe to say that all the difficulties encountered in the management of chronic duodenal ulcer stem from the fact that the cause of the ulceration is not known with any degree of certainty. We can produce peptic ulceration in experimental animals and we believe we know some of the factors which influence the course of the disease in the individual patient, but that is far from knowing the exact cause of ulcer in all patients. The problem is further complicated because the factors which produce the disease originally may not be responsible for its persistence. Furthermore, all the factors believed to be important may be present in an individual who never develops an ulcer. Both experimental and clinical evidence reveals that psychogenic, neurogenic, chemical, motor, vascular (local hyperæmia and infective emboli) and hormonal factors may be involved in the causation and chronicity of duodenal ulcer and that these factors may be implicated in varying degrees in an individual case.

With psychogenic and neurogenic factors receiving so much attention recently, it is interesting to note that Rokitanski of Vienna propounded the neurogenic theory of the origin of peptic ulceration more than a century ago, in 1841. The evidence on which the neurogenic hypothesis is based is, first, the existence of cerebral lesions and peptic ulcer in the same individuals; second, the occurrence of peptic ulceration in the œsophagus, stomach and duodenum in infants following cerebral injury at child birth; and thirdly, the experimental evidence showing that induced vagal and sympathetic disturbances will produce peptic ulcers in animals.

In 1868, Hoffman reported a patient who had died from a perforation of a gastric ulcer and who was suffering also from a tumour invading the pons and the medulla. Burdenko and Mogilnitzki,[1] in 1925-26, claimed to have produced gastric erosions and perforations and, in some instances, chronic gastric ulcers experimentally by puncturing the hypothalamus. Cushing's[2] report (1932) of eleven cases of intracranial lesions associated with gastric or duodenal ulceration, supported isolated accounts of such associated diseases and further stimulated an interest in the neurogenic theory which has been maintained until the present time. In 1941, the late Dr. Sarah Meltzer and the author reported a case of intractable gastric ulcer with final malignant change associated with a benign tumour of the brain. Much experimental evidence of the effects of actual or relatively increased vagal activity has been forthcoming. Manning, Hall and Banting[3] in 1937, showed that prolonged vagal stimulation gave rise to areas of hæmorrhage and congestion in both stomach and duodenum. Atropine prevented such lesions, whereas eserine accentuated the changes which led to ulcer formation. It has also been reported by a number of observers that division of the sympathetic pathways to the stomach and thus uncontrolled vagal action will lead to the development of gastric erosions and ulceration. All these are but a few of the numerous experiments carried out to indicate the importance of the neurogenic factor and the rôle of the vagus. Adding the grain of salt, one might, of course, observe that the occasional association of peptic ulceration with an intracranial tumour, is well within the bounds of coincidence. Wherever the truth regarding the nature of the stimulus lies, it is not to be denied that the classical experiments of Mann and Williamson[4] in 1923 have shown the important rôle played by the acid gastric juice in ulcer formation. Code and Varco[5] in 1940 further emphasized the importance of continuous acid gastric secretion in producing peptic ulceration which they induced by the intramuscular implantation of histamine in beeswax.

With this evidence before us, it is well to ask, what does it represent in terms of actual knowledge in the treatment of the individual sufferer from chronic duodenal ulcer? In animals, we can at least ignore the central factors and produce ulcers through the play of local factors. Again, in experimental animals, we can bring the central factors into play by stimulating the vagus and producing hyperæmia, hypersecretion, hypermotility, and ulceration without any previous change in the local mechanism. It would seem rational to believe that in the individual sufferer from chronic duodenal ulcer a chain of events arises which can be initiated or influenced profoundly by any one of several fac-

tors. One influence may play a dominant rôle in one patient, another may be more important in the next. It also seems evident from all this information that while one factor may be predominantly responsible for the production of the original mucosal defect, other elements or a combination thereof explain the chronicity of the ulcer. In other words, the acid-chyme erosion factor, initiated or aggravated by neurogenic impulses, may have actually caused the mucosal lesion in an area already rendered temporarily vulnerable by local congestion or by a septic embolus containing non-hæmolytic streptococci, while a disturbed motor mechanism may be responsible to a large measure for the pain and chronicity of the lesion. I must confess, however, that such a hypothesis, while it may form the basis of an argument, does not produce a wholly satisfactory solution to the complicated question of etiology. The best that can be said for the whole problem, I believe, is that a vicious cycle has been set in motion and that if this cycle can be interrupted in one or more places, by medical or surgical measures, the course of the disease can be markedly altered. These measures to be effective must take into consideration both the neurogenic and the combination of chemical, motor and hormonal factors.

When I served my apprenticeship in surgery, the surgical treatment of chronic duodenal ulcer consisted of a simple posterior gastro-jejunostomy under all circumstances. This was at a time when surgeons with wide experience stated categorically that chronic duodenal ulcer was primarily a surgical disease while no less eminent internists were equally categorical in their belief that the disease was a medical problem. At that time, the entire medical treatment consisted of frequent feedings, chiefly of milk, together with the administration of alkalis. At this time also, the surgeon had little more to offer than a posterior gastro-enterostomy. In other words, the entire attack on the problem by both physicians and surgeons was a local one, based respectively on the satisfactory experience of simple dietary and medical measures in uncomplicated cases, and on extremely satisfactory results from posterior gastro-enterostomy for chronic duodenal ulcer with marked pyloric obstruction.

Just before 1930, a radical change in attitude took place. It occurred chiefly because the surgeon began to realize that posterior gastro-enterostomy, which had been sponsored with enthusiasm by such eminent surgeons as Moynihan, William and Charles Mayo, Sherren, Oschner, Murphy, Balfour, Crile and many other outstanding men, was inadequate in solving the problem. Furthermore, it was realized that this procedure, in itself, was adding another problem, that of anastomotic ulcer (the incidence of which was greatly under-estimated), a more serious and difficult condition to control than the original lesion.

At this period, too, renewed interest in local pyloroplasty became evident. The Finney operation, devised originally in 1902, was revived. The Heineke-Mikulicz type of pyloroplasty, in which the incision began in the stomach and was carried through the pyloric ring and into the duodenum and then the incision sutured in the opposite direction, was an attempt to enlarge the pyloric canal and obliterate pylorospasm, which was thought to produce an effective barrier between the acid of the stomach and the alkaline secretions of the duodenum. Starr Judd, of the Mayo Clinic, modified both the Finney and the Heineke-Mikulicz (Horsley) procedures by excising the anterior two-thirds of the pyloric sphincter and suturing the anterior wall of the stomach and duodenum together. A further modification advocated by Wilkie of Edinburgh was infra-papillary gastro-duodenostomy (Kocher's) in which the second and third parts of the duodenum were mobilized and anastomosed to the stomach in such a manner that the acid contents of the stomach would impinge directly on that portion of the duodenum into which the highly alkaline secretions of the pancreas and liver were being delivered. It is obvious that these measures were planned to do two things: first, to overcome pylorospasm; and second, to utilize natural alkaline secretions to neutralize the hyperacidity of the stomach. In other words, an internal pharmacy was provided to obviate frequent visits to the corner drug-store.

The acceptance of these pyloroplastic procedures must be taken as evidence that a duodenal ulcer was considered a local and limited disease in the same sense that appendicitis or basal cell carcinoma of the skin is now considered a local condition. How erroneous this conception was can be emphasized by the fact that there was re-activation of the ulcer in over 22% of my series of 44 cases within two years.[6] The

period was short-lived also because it was soon proved that these procedures had little effect on either the emptying time of the stomach or the level of gastric acidity.

Shortly after 1930 and particularly after the publication of Cushing's paper in 1932, a reorientation by the profession took place with regard to its attitude towards the etiology and treatment of duodenal ulcer, and many changes occurred which have had a beneficial effect on the patient. In the first place, the realization was born that local factors were not the all important consideration, at least in the initial stages of the disease. Secondly, adequate medical treatment should include not only relief of symptoms but the adjustment of the individual's life and habits in such a way that though one could not guarantee against recurrence, one could at least reduce the frequency and severity of subsequent attacks and thereby lessen the danger of serious complications. A third change involved the understanding by the profession as a whole, including the surgeons, that in the initial phases of duodenal ulcer, it was a medical and not a surgical problem. Finally, it was accepted that posterior gastro-enterostomy as a routine procedure, except in the presence of cicatricial stenosis, failed to relieve the symptoms of the original ulcer or was followed by a disturbingly high incidence of anastomotic ulceration, particularly in the young, nervous patient with high acid level. In other words, it did not provide the safe answer for the young, active patient during a period of his life, when it was especially necessary for him to assume heightened responsibilities both at home and in business.

Having eliminated 80% of duodenal ulcers from consideration as far as surgery is concerned, we should examine and evaluate the surgical problems in those patients in whom medical treatment has partially or completely failed. In considering any series of cases selected for surgery on this basis and comparing the results of treatment, it is obviously quite unjustifiable to compare the results of such surgical treatment with the results of medical treatment in the first 80%. If surgery can reclaim 80 to 85% of that small proportion of patients who have failed to respond to adequate medical therapy, then it has justified the radical nature of the treatment in these selected cases. At this junction, it is fitting to acknowledge that the good results and the low mortality are in no small measure due to the fine advances in anæsthesiology and the recognition and correction of the secondary effects of the disease by modern medical measures.

At present, we have two operative procedures which radically change the physiology of the stomach. Both operations are based on sound experimental and clinical observations. It is fortunate that nature so often provides us with more than one solution to the problem of wound healing and recovery. At the present state of our knowledge, it is not a question as to whether an excision of the lower three-quarters of the stomach together with the duodenal ulcer or a vagotomy plus posterior gastro-enterostomy is the superior method. The final answer to this problem is not available and will not be available probably for another five years or even more. It should be stated that the majority of experienced gastric surgeons on this continent, as well as in Europe, believe that radical resection of the stomach still offers the patient the best chance of recovery. This opinion is based on a great deal of personal experience and one must give such opinions first consideration. However, the newer operation of vagus resection with or without gastro-enterostomy has, in the short period of four years seriously challenged the preference for the more radical procedure. This is based not only on the excellent immediate results but because it has been developed and sponsored by men who are leaders both in experimental and clinical fields as well as by surgeons of good judgment and undisputed technical ability. The Dragstedt[7, 8, 9, 10] operation, if not the final or complete solution, may at least be the second best choice in a difficult situation and, in my opinion at least, it has made a very worth-while contribution to the study and treatment of chronic, intractable duodenal ulcer. The most enthusiastic proponents of gastric resection still admit that some 10 to 15% are unrelieved. This may be due to the dumping syndrome, to stoma ulcer or to hypoglycæmia with shock. In others, postoperative gastritis, anæmia, hæmorrhage, nervous and cardiovascular symptoms, which sometimes develop or continue after this operation may be due to factors not related to the initial disease or the operation itself, but rather to the patient's unstable disposition. While vagotomy will not solve all the problems related to the complications which may follow

gastric resection, I think it will markedly influence some of the more important ones, particularly those relating to anastomotic ulcer and bleeding.

It is said that posterior gastro-enterostomy is the perfect operation for chronic duodenal ulcer of long standing in cases where fibrous stenosis has developed with marked gastric retention and stagnation, often associated with gastritis and lowering of gastric acidity. It just happens that many of these consequences, that seem so desirable in the patient who responds to gastro-enterostomy for pyloric stenosis are also reproduced by vagus resection.

Although partial vagus resection had been practised as early as 1938, combined with subtotal gastrectomy for ulcer by Winkelstein and Berg[11] with good immediate results, no general interest in the method developed until Dragstedt reported his initial experiences. These depended partly upon the earlier work of Carlson. Carlson had refuted the experimental evidence of Pavlov that gastric secretion depended solely upon the sight of food and its presence in the stomach. Carlson showed that there is a constant flow of hydrochloric acid throughout the entire twenty-four hours, and Winkelstein pointed out that patients with ulcer are more likely to demonstrate elevated acid values in night secretion than individuals without ulcer. In his experimental work, Dragstedt showed he could prevent anastomotic ulcer which occurs in 95% of Mann-Williamson dogs by resecting their vagus nerves. Furthermore, by isolating whole stomachs of dogs, with the vagus nerves intact, he found ulcer formation was common after histamine, but if the isolated stomach was deprived of its vagus innervation, a reduction in gastric secretion and no ulceration resulted.

The rationale of the Dragstedt operation depends upon the importance of the rôle of gastric hydrochloric acid in ulcer production and the fact that secretion of this acid is continuous and in certain individuals is more marked during sleep when it is not neutralized by food or alkaline medication. It is based also on the knowledge that excess of gastric secretion may be induced by organic or psychic stimulation of the vagal nuclei in the mid-brain. Thus Dragstedt hoped to decrease the night flow by vagal denervation of the stomach while at the same time reduce the hypermotility of the stomach and spasm in the duodenum which is no doubt one of the causes of ulcer pain. The success of his method has been obvious from the consideration of results not only of his own cases but of those of surgeons in other quarters who have adopted his procedure. (Grimson,[12] Orr, and Johnson,[13] etc.)

In the concluding portion of this discussion, I wish to consider the position of vagotomy from our experience at the Winnipeg Clinic with this procedure. We continue to maintain a keen interest in the operation and its results. All cases of duodenal ulcer requiring surgery are not subjected to this operation. Approximately half of our cases are undergoing partial gastrectomy without interfering with the vagus nerves. A comparative review, after the elapse of five years or more, may help us to decide as to relative merits of the two procedures.

The first of our cases underwent vagotomy in May, 1946. During the intervening 18 months, 63 cases have undergone vagotomy. The great majority of these cases have been operated upon by Drs. M. B. Perrin and K. R. Trueman, who have been particularly interested in this surgical approach to the problem of duodenal ulcer. All of the patients have been carefully selected for surgery by members of our medical department and much of the pre- and post-operative study and investigation has been supervised by one of our gastro-enterologists, Dr. Wendell Macleod. In the largest proportion of the early cases operation was performed above the diaphragm, the exceptions being those cases with obstruction due to pyloric stenosis. These latter cases were done through the abdomen combining sub-diaphragmatic vagotomy with posterior gastro-enterostomy. At this stage, the supradiaphragmatic approach was favoured because of the relative simplicity of the method and the opportunity it provided to study the effects of what might be described as a "pure" vagotomy. It was felt that more would be learned from the procedure if it was performed alone and not supplemented by some other operation. Because of the apparent good results and freedom from complications, a further number of cases were so treated. In this way, the vagotomists at the Clinic were able to establish, by thorough section of the main vagus nerves and the available intervening fibres, that the quality and quantity of gastric hydrochloric acid could be controlled. In this matter, they have depended largely upon the comparison of the pre- and post-operative values in gastric

analysis in the fasting state and after the administration of insulin. It was also found that the greater proportion of these cases were relieved of their ulcer symptoms and were restored to their normal pursuits after a relatively short convalescence. In some cases, the ulcer crater was not demonstrated a short time after operation. In others, it is difficult to determine this because of the atony of the stomach and failure of barium to leave it during the fluoroscopic portion of the examination. It was during the early part of our experience that some difficulties resulting from supradiaphragmatic vagotomy were encountered. These have already been reported by others and will be described in detail in a later review of our results. They are chiefly the postoperative gastric retention, which was marked enough in some instances in the x-ray film to be alarming, and the pain in the chest at the site of the incision.

Practically all our "pure" vagotomies developed gastric stasis. The two cases failing to do so were considered as incomplete nerve sections and this judgment was supported by the normal response of gastric secretion to insulin in addition to the persistence of the patient's symptoms. In a large proportion, there is 40 to 75% retention at five hours but serial plates at six, seven, eight and twelve hours revealed most of the barium out of the stomach. It is surprising what little discomfort was associated with even the most marked and prolonged cases of retention. However, loss of appetite, eructations and even vomiting occurred occasionally. The retention has been found to lessen gradually as time elapses. The reason why retention should be more marked in some cases is probably explained on the basis of the amount of scar tissue at the pylorus, the result of the activity of the ulcer. Normally, the extraordinary motility of the stomach, characteristic of the patient with an ulcer, can compensate for some degree of narrowing due to fibrosis. However, once this force is eliminated by the vagotomy, the pyloric opening is not sufficiently large to permit free emptying of the stomach.

As it is not always possible to foresee which cases will develop undue retention and because it is felt that anastomotic ulcer will not complicate a gastro-enterostomy protected by vagotomy, we are now following the example of Dragstedt and others by doing a subdiaphragmatic vagotomy and posterior gastro-enterostomy. It should be stated here that, in our experience, in only one case was retention sufficiently persistent and complete to demand gastro-enterostomy as a subsequent procedure to transthoracic vagotomy. Certainly the abdominal route gives the further advantage of exploring its contents and correcting other abnormal states.

Anastomotic ulcer, which is definitely a surgical problem and usually a troublesome one, has been treated in two instances by trans-thoracic vagotomy alone with excellent results. A case of gastro-jejuno-colic fistula also underwent a supradiaphragmatic vagotomy (May, 1947). Ordinarily, we have performed a hepatic flexure colostomy proximal to the lesion to divert the fæcal stream and reduce contamination as advocated by Pfeiffer.[14] In this case, a preliminary colostomy was not done. Later, at laparotomy, it was interessting to note, in this case at least, little œdema and inflammatory reaction at the site of the fistula. However, it should be added that a hæmorrhage followed the preliminary operation of vagotomy after two weeks. This is the only instance of hæmorrhage after vagotomy in our series.

I should like to report our experience also with other associated difficulties after vagotomy. Dysphagia occurred in five cases, all of which had the supradiaphragmatic operation and in whom the œsophagus was handled as is necessary during the nerve dissection. It was transient in all cases but one individual required dilatations. Five of our cases developed some diarrhœa and two of these had as many as ten to twelve movement a day. This condition also corrected itself with the passage of time. It is interesting that several cases of chronic constipation reported the pleasure of a regular daily evacuation after vagotomy.

As I have said, it is too early to judge vagotomy as an individual or part of a combined procedure in the treatment of chronic duodenal ulcer. However, it is my impression that it is a further weapon in the armamentarium of the surgeon in the care of this disease. Certainly, it is a useful alternative to gastric resection where the latter is impractical or perchance impossible by reason of local involvement or infirmity of the patient. It is the procedure of choice in anastomotic ulcer and as a supplement to gastro-enterostomy for pyloric stenosis. It will also be a useful adjuvant to gastric resection in the young, active man with excessive gastric secre-

tion and perhaps will permit a less extensive removal of the stomach without fear of the consequences of an anastomotic ulcer.

Possibly the greatest value of vagotomy lies in the treatment of an ulcer which is uncomplicated by penetration, bleeding or stenosis and which has failed to respond or be controlled by medical therapy as opposed to the complicated ulcer for which a sub-total gastrectomy continues to be the best method of management or as an adjunct to a partial gastrectomy of gastrojejunostomy. Finally, vagotomy has been shown to be useful in relieving epigastric pain due to such pathological conditions as pancreatitis and pancreatic calculi. It is suggested here that its further use may be in the relief of pain that is sometimes associated with inoperable malignant ulcers* of the stomach.

REFERENCES

1. BURDENKO, N. AND MOGILNITZKI, B.: *Ztschr. f. d. ges. Neurol. u. Psychiat.*, **103**: 42, 1926.
2. CUSHING, H.: *Surg., Gyn. & Obst.*, **55**: 1, 1932.
3. THORLAKSON, P. H. T. AND MELTZER, S.: *Ann. Surg.*, **113**: 521, 1941.
4. MANNING, G. W., HALL, G. E. AND BANTING, F. G.: *Canad. M. A. J.*, **37**: 314, 1937.
5. MANN, F. C. AND WILLIAMSON, C. S.: *Ann. Surg.*, **77**: 409, 1923.
6. CODE, C. F. AND VARCO, R. L.: *Proc. Soc. Exper. Biol. & Med.*, **44**: 475, 1940.
7. THORLAKSON, P. H. T. AND HAY, A. W. S.: *Canad. M. A. J.*, **45**: 298, 1941.
8. DRAGSTEDT, L. R. AND OWENS, F. M. JR.: *Proc. Soc. Exper. Biol. & Med.*, **53**: 152, 1943.
9. DRAGSTEDT, L. R., PALMER, W. L., SCHAFER, P. W. AND HODGES, P. C.: *Gastroenterology*, **3**: 450, 1944.
10. DRAGSTEDT, L. R. AND SCHAFER, P. W.: *Surgery*, **17**: 742, 1945.
11. DRAGSTEDT, L. R.: *Canad. M. A. J.*, **56**: 133, 1947.
12. WINKELSTEIN, A. AND BERG, A. A.: *Am. J. Digest. Dis.*, **5**: 497, 1938.
13. GRIMSON, K. S., TAYLOR, H. M., TRENT, J. C., WILSON, D. A. AND HILL, H. C.: *South. M. J.*, **39**: 460, 1945.
14. ORR, I. M. AND JOHNSON, H. D.: *The Lancet*, **2**: 84, 1947.
15. PFEIFFER, D. B. AND KENT, E. M.: *Ann. Surg.*, **110**: 659, 1939.

* One patient, Mrs. N., aged 39, who was found at operation to have an inoperable carcinoma of the stomach and who had been suffering considerably from epigastric pain, was relieved completely insofar as the pain was concerned following subdiaphragmatic vagotomy. The operation was done on November 8, 1947 and relief of the epigastric pain has continued until the present time (January 20, 1948).

INSECTICIDAL SOLUTIONS.—Various insecticidal dusts and sprays have proved highly effective in the householder's war against insects and other pests but such agents include potentially dangerous chemicals including lead arsenate, basic copper arsenate, paris green, cyanide and fluoride compounds, sulphur and nicotine. The poisonous effect of each of these insecticides varies according to the nature of its chemical composition but prolonged contact with most of them may have harmful effects. Care should therefore be taken when handling all such toxic materials.

OSTEOID OSTEOMA*

J. E. Pritchard, M.D. and J. W. McKay, M.D.

Montreal, Que.

THE osteoid osteoma is a small but usually painful, tender and troublesome benign lesion of the bones. It has often been mistaken for other conditions such as chronic osteomyelitis, cortical abscess, bone abscess with sequestrum, Brodie's abscess, sclerosing osteitis, osteochondritis dissecans, tuberculosis, bone cyst and even sarcoma, with the result that it sometimes has been improperly treated even to the extent of unnecessarily extensive resections or amputations. It is important therefore that it be recognized for the benign tumour that it is, and to know that it can be cured promptly and easily by complete local removal.

This tumour was first presented as an entity and named osteoid osteoma by Jaffe, pathologist to the Hospital for Joint Diseases, New York, in a report of 5 cases published in 1935.[1] In two subsequent reports by Jaffe and Licktenstein[2] and by Jaffe[3] from that same source, published in 1940 and 1945 respectively, 57 more cases were recorded. These three very excellent papers give a thorough analysis of all aspects of the disease.

That this lesion is a distinct entity and a tumour we must agree with Jaffe. We feel that there is no longer any point in discussing why it is not an inflammatory one. The differential diagnosis between osteoid osteoma and certain other lesions of bones, especially abscess, we must admit is not always easy without the aid of histologic sections. However, as one becomes familiar with the clinical behaviour and the radiographic appearances of this disease, a correct diagnosis can nearly always be made before operation. Even in doubtful cases, exposure of the lesion should enable the surgeon to recognize its true nature.

Prior to Jaffe's original article there were published under other titles a number of case reports[4, 5, 6, 7] examination of which leaves no doubt that the lesions described are the same as Jaffe's osteoid osteoma. Since then several papers by other authors have been published under the title of osteoid osteoma.[8 to 20] All these reports indicate that the osteoid osteoma is by no means infrequent. From the single source, the Hospital for Joint Diseases mentioned above, 62 cases were reported between the years 1935

* From the Departments of Pathology and Radiology, McGill University and the Montreal General Hospital.

and 1945. In a general hospital no such large numbers are likely to be found.

In our own experience in the past 18 years, 19 of these tumours have been encountered, 8 are recorded in the files of the Montreal General Hospital, 6 were shown to us by our pathologist colleagues in Montreal, and sections of 2 and radiographs of 3 were sent from outside sources for an opinion. Of these 19 cases, 15 are selected for this report.

CASE 1

A young woman of 26 first noticed pain and swelling in the proximal phalanx of the middle finger of the right hand in 1936. This gradually increased and in February, 1939, she consulted her doctor because of the very troublesome pain which disturbed her sleep. Joint movements were good. There was no history of trauma. A radiograph made at that time outside the hospital was reported as osteitis and bone abscess containing a sequestrum. The swelling and pain increased and on May 15, 1939, she was admitted to the Montreal General Hospital. The x-ray film accompanying the patient was interpreted as osteoid osteoma (Fig. 12).

Operation revealed a very hard, rounded, pea-sized nodule in the cancellous bone near the distal end of the diaphysis. This was removed easily with the curette and the cavity was thoroughly curetted. The specimen received in the laboratory consisted of a 5 mm. pearl-gray, finely jagged, rounded body of the consistency of hard bone. Histologically it was typical of osteoid osteoma with atypical lamellar bone formation. The pathological diagnosis was osteoid osteoma.

Following the operation there was immediate relief of the troublesome pain. A month later, examination showed a good functioning finger and no symptoms. On May 26, 1947, 8 years after operation, the patient was again examined. There were no symptoms and the finger functioned perfectly. A radiograph showed restitution of the bone with the exception of a slight notch at the site of operation. The other bones of the hand which

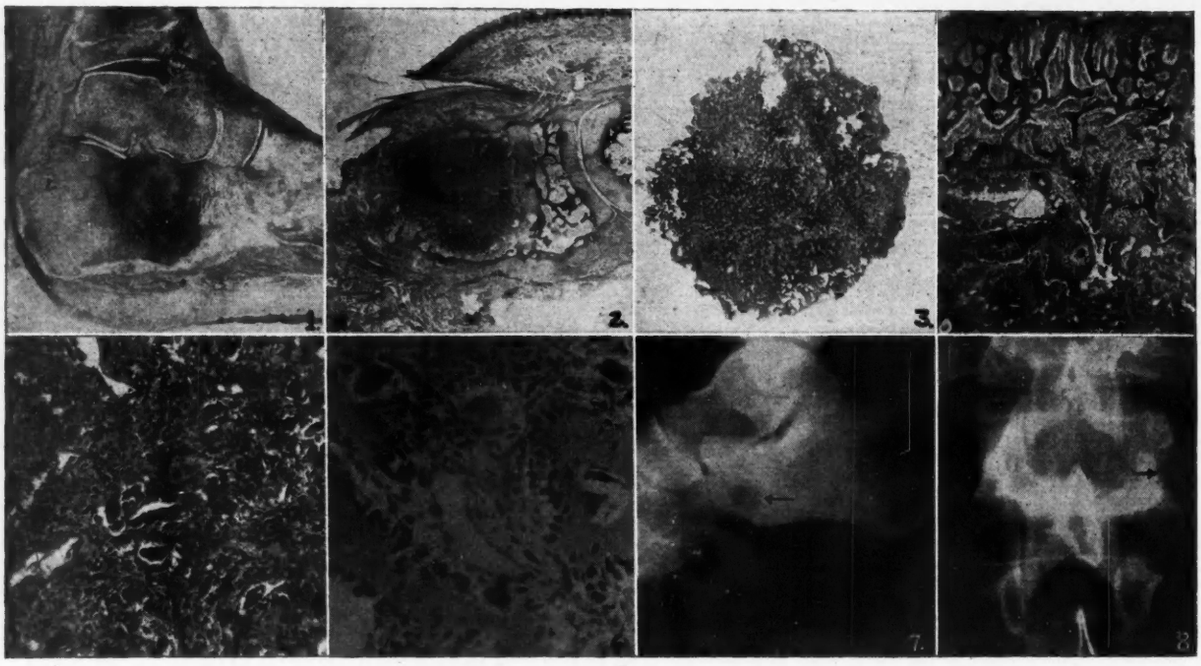


Fig. 1. (Case 4).—Longitudinal section through the foot showing the 4.5 x 4 cm. circumscribed tumour in the anterior end of the os calcis. In it are areas of hæmorrhage. **Fig. 2.** (Case 3).—Photomicrograph x 3 of a longitudinal section of the toe showing the sharply demarcated rounded and finely trabeculated body occupying the whole of the medulla of the diaphysis of the distal phalanx. The epiphysis is intact. Note the thin cortex above and below and its complete absence distally. Between the tumour and the cortex there is a pale zone of connective tissue. **Fig. 3.** (Case 2).—Photomicrograph x 10 of the tumour removed by the curette. It is composed of finely meshed trabeculæ of calcified osteoid in a substrate of osteoblastic connective tissue. **Fig. 4.**—The periphery of the tumour shown in Fig. 2. The margin of the osteoid osteoma is seen along the lower border and the cortex along the upper border. The area between the tumour and the cortex is occupied by a well vascularized connective tissue in which are a few osteoid trabeculæ. The cortex shows marked lacunar absorption and replacement by connective tissue. The periosteum is very cellular and there is new periosteal bone formation. **Fig. 5.**—A small area of the tumour shown in Fig. 2. It shows the basic osteoblastic type of tissue, well vascularized and containing many multinucleated giant cells. There are many small irregular deposits of osteoid but no formed trabeculæ. Elsewhere in this tumour osteoid trabeculæ, as in Fig. 6, are abundant. **Fig. 6.**—The tumour illustrated in Fig. 1. It shows well the non-calcified osteoid trabecular with intervening well vascularized osteoblastic type of connective tissue containing numerous giant cells. This is the non-calcified stage. **Fig. 7.** (Case 10).—The head of the os calcis shows a roughly rounded area of radiotranslucency, the non-calcified stage of the tumour. **Fig. 8.** (Case 9).—Marked rarefaction of the transverse process of the vertebra; at its base there is a small rounded radiotranslucent area surrounded by a rim of condensed bone, the non-calcified stage of the tumour with reactive bone formation surrounding it.

previously showed marked general rarefaction had returned to normal.

CASE 2

A young woman of 24 years, was admitted to the Service of Dr. S. E. Goldman at the Jewish General Hospital, Montreal, on October 16, 1935, complaining of pain of 15 months' duration in the right ankle on walking and on everting the foot. At times the ankle swelled and was tender. A radiograph (Fig. 11) was diagnosed as Brodie's abscess. At operation, a pea-sized dense bony nodule was easily removed. There was no pus. The specimen received in the laboratory consisted of a rounded, brown, 5 mm. nodule of bony consistency. Microscopically (Figs. 3 and 9) it was a typical osteoid osteoma.

This patient was in the Massachusetts General Hospital, Boston, in March, 1935, 7 months prior to operation and 7 months after the onset of symptoms. An x-ray examination at that time was reported as showing general rarefaction of the bones of the foot and no localized lesion. Following operation there was prompt relief of symptoms and the patient is still free of symptoms 12 years after operation.

CASE 3

A boy of 13 was admitted to the Montreal General Hospital on March 10, 1939, complaining of a sore,

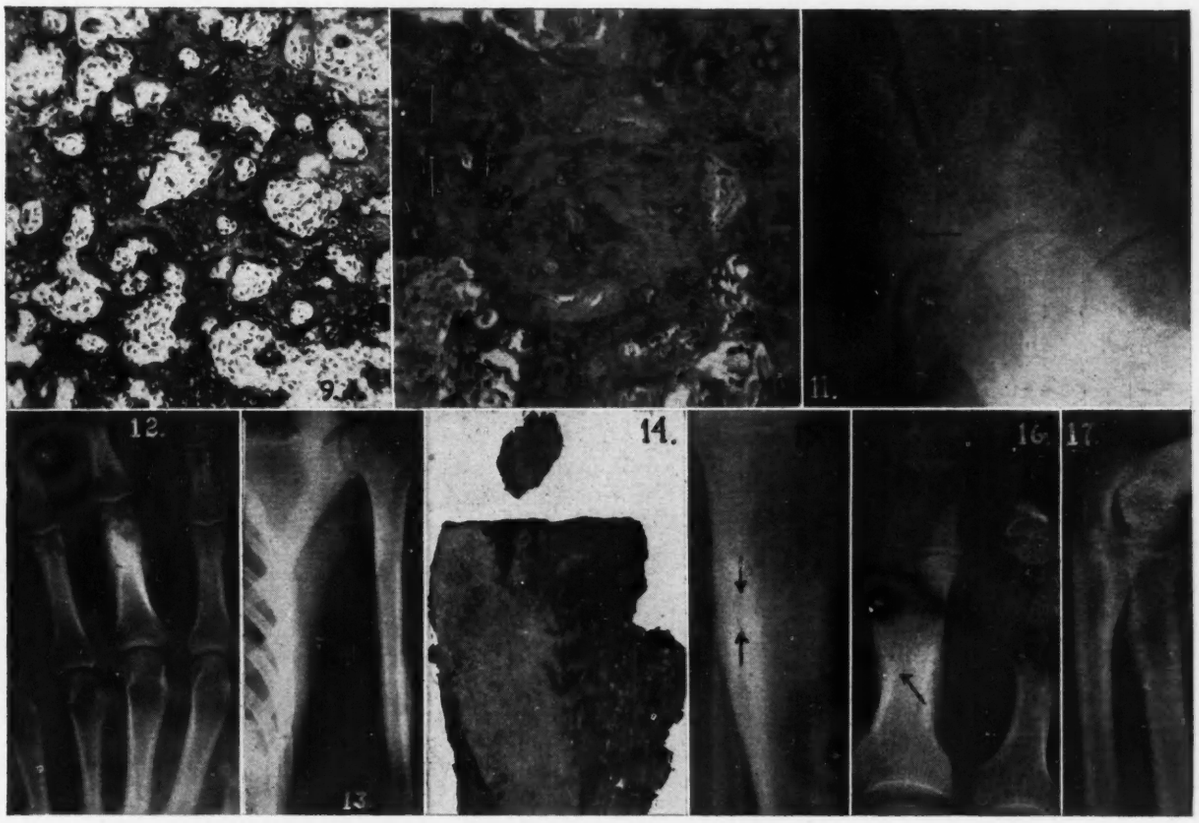


Fig. 9.—Higher power photomicrograph from the centre of the tumour shown in Fig. 3. There is a meshwork of calcified osteoid trabeculæ in the interstices of which there is a moderately cellular and moderately vascularized connective tissue and only a few giant cells. This is the calcified stage later than in Fig. 6. See Fig. 11. **Fig. 10.** (Case 1).—Photomicrograph of the tumour showing massive calcified osteoid and some lamellar bone formation. The interstices are narrow and filled with poorly vascularized connective tissue. Giant cells are very scanty. This is the still later calcified and ossified stage. See Fig. 12. **Fig. 11.** (Case 2).—Radiograph showing in the navicular bone a rounded area of radio-translucency with a large central rounded moderately opaque body. The bones generally are rarefied. The opaque nodule after removal is shown in Figs. 3 and 9. **Fig. 12.** (Case 1).—Radiograph showing in the distal end of the first phalanx, a very dense rounded body surrounded by a zone of radio-translucency. About the tumour and extending proximally the bone is condensed and thickened. There is general rarefaction of the other bones. **Fig. 13.**—Preoperative radiograph showing periosteal bone formation and in the cortex the small rounded radio-translucent zone. A small central opaque core overlaid by the dense cortex can be identified with difficulty. **Fig. 14.** (Case 14).—Photograph x 3. The larger mass represents the thickened condensed cortex. The smaller one is the osteoid osteoma which separated easily when the bone was being chiselled away. See Fig. 15. **Fig. 15.** (Case 14).—Lateral view showing the marked cortical condensation and thickening posteriorly in the tibia. In the thickened cortex can be seen very faintly, the oval dense body surrounded by a narrow zone of radio-translucency. **Fig. 16.** (Case 10).—Radiograph showing marked cortical thickening and condensation of the shaft of the proximal phalanx of the toe. Along the medial margin where condensation is greatest, there is rough periosteal bone formation. Beneath this area in the deep margin of the cortex the little tumour is scarcely visible. Note the rarefaction of the rest of the bone. **Fig. 17.** (Case 12).—Radiograph showing the radio-translucency in the tubercle of the radius and the translucent tract extending through the cortex. There is overlying periosteal bone formation with faint condensed streaks at right angles to the surface.

swollen toe for two months. Examination showed a bulbous, tender swelling of the distal phalanx of the second toe of the right foot. There was no history of injury. The temperature was normal and there were no other symptoms but he was considered to have a rheumatic heart. The Mantoux test was 4 plus. The clinical impression was tuberculous osteomyelitis. An x-ray examination was reported as showing marked swelling of the soft tissues and decalcification of the bone of the distal phalanx without any breakdown of bone. The chest x-rays were negative. On a diagnosis of tuberculosis, the toe was amputated through the middle joint on March 16, 1939. A longitudinal section through the specimen (Fig. 2) shows swelling of the soft tissues and in the diaphysis of the distal phalanx, a rounded, reddish, tough body. The epiphyseal cartilage is intact. The cortex is thinned by absorption from within. The gross appearance is typical of osteoid osteoma. Histologically it was also typical osteoid osteoma. The boy was alive and well 8½ years after operation.

CASE 4

A boy of 14 years was admitted to the Montreal Hospital on September 22, 1928, complaining of sharp pain and swelling of one month's duration in the region of the external malleolus. Four months previously he had twisted his ankle with no ill-effects other than slight soreness for a few days. Examination revealed a tender swelling on the lateral aspect of the ankle. X-ray examination on September 28, 1928, was reported as showing swelling of soft parts, decalcification of the bones of the foot and leg, indistinctness and slight loss of joint spacing and no evidence of fracture or of localized destructive or productive bone changes suggestive of tuberculosis. The tuberculin and blood Wassermann tests were negative. His temperature ranged up to 99.2°. There were no other significant signs or symptoms. A cantilever cast was applied with some relief of pain and he was discharged on October 8, 1929. Two months later on December 16, 1928, and four months after the onset of symptoms, he was re-admitted with increased pain and swelling. Movements at the ankle were limited. X-ray examination on December 29, 1928, was reported as follows: "There is evidence of productive and destructive bone change involving the anterior end of the os calcis and extending into the joint which is suggestive of new growth. There is marked rarefaction of all bones in this film". Blood leucocytes numbered 8,200 to 9,000. Hgb. 80%; blood Wassermann negative. Enlarged inguinal glands appeared on December 29, 1928. One of these was removed and reported pathologically as catarrhal lymphadenitis and no tumour. His temperature during the second admission was normal with the exception of a rise to 100° on January 14, 1929. The condition in the foot was considered a malignant tumour so an amputation was done through the lower third of the leg on January 17, 1929.

The specimen (Fig. 1) cut longitudinally in the antero-posterior plane shows in the anterior end of the os calcis a 4 x 4.5 cm. roughly rounded, firm, pink mass replacing the cancellous bone and cortex and bulging into the joint. It was sharply circumscribed but not encapsulated and in it there are small hæmorrhagic areas. The pathological diagnosis originally was osteogenic sarcoma but on review of the sections 6 years later, the diagnosis was altered to osteoid osteoma of which it is a good example. This patient was alive and well 18 years after operation.

CASE 5

A woman of 36 years had had a painful swelling of the anterior end of the mandible for 2 years. Because of the pain she consulted her doctor in September, 1936. No x-ray examination was made. The condition was thought to be a bone cyst or an unerupted tooth. On cutting down on the lesion the surgeon encountered tough, gritty tissue, "like spongy bone", in the cancellous part of the mandible. The whole was excised along with a margin of cortical bone. The material sent to the Montreal General Hospital consisted of a 2 x 1.3 cm. triangular piece of tough gritty, grayish pink tissue and a small fragment of attached hard bone. The pathological diagnosis was osteoid osteoma.

A letter from this woman in June, 1945, 11 years after operation reported no symptoms and no recurrence of the swelling.

CASE 6

The only information available is that this man of 24 years had had a painful patella for several months. A radiograph was submitted to the x-ray department of the Montreal General Hospital for diagnosis. It showed in the patella a small rounded area of rarefaction with its densely calcified core characteristic of osteoid osteoma. The radiologic diagnosis was osteoid osteoma. No further information has been obtained.

CASE 7

Male, aged 44, injured the right knee in a fall on March 20, 1947. He visited the Out-patient Department the next day complaining of pain in the knee on flexing the leg, only since the accident. There was tenderness over the lateral aspect of the knee. A radiograph showed in the patella near the articular surface a 7 x 5 cm. rounded area of rarefaction in the centre of which there was a densely calcified rounded body. The radiologic diagnosis was osteoid osteoma. The tumour development must have preceded the injury and symptoms, and therefore must have reached this advanced stage without symptoms. This man ignored advice to return to the hospital for further examination.

CASE 8

A girl of 20 years complaining of swelling, slight stiffness and limitation of movement of the right knee of two years' duration, consulted Dr. W. O. Rothwell of Temiskaming, about November 1, 1947. There was no point of tenderness and no complaint of pain and no history of injury. The quadriceps muscles showed considerable atrophy. A radiograph sent to the Montreal General Hospital for an opinion revealed in the patella near the anterior surface a small area of radio-translucency with a dense central core typical of osteoid osteoma.

Because of the minor degree of symptoms the orthopædic surgeon consulted advised no surgical interference. After about one month's treatment with active exercises, her doctor reports that there is now full movement at the knee and the swelling is diminishing.

CASE 9

A boy of 19 years was admitted to the service of Dr. R. C. Laird at the Toronto Western Hospital in June, 1946, complaining of pain of unstated duration, radiating from the right costo-vertebral angle into the right flank. The pain seemed to be of root neuritis type. The radiograph (Fig. 8) shows rarefaction of the right transverse process of the first lumbar vertebra. At the base of the process is a small round radio-translucent spot about which there is a narrow rim of condensed bone. There is no calcified core.

The transverse process was removed. The histological sections sent to us by Dr. George Shanks, then pathologist to that hospital, are typical of osteoid osteoma without calcification of the osteoid. Following the operation relief of pain was prompt and has remained so up to the latest report one year after operation.

CASE 10

A man of 25 years consulted his doctor about November 1, 1947, because of soreness in the foot toward the end of the day. Inversion of the foot caused pain over the lateral aspect and there was tenderness on pressure over the head of the os calcis. There was no swelling. His general health was good. A radiograph (Fig. 7) shows a 1.5 cm. ovoid, sharply demarcated area of radio-

translucency in the head of the os calcis. There is no central condensation although there is a little irregularity in the density of the lesion. The radiologic diagnosis was osteoid osteoma. It represents the non-calcified stage of the tumour. Removal of the tumour has been recommended, but has not yet been done.

CASE 11

A 36-year old man was admitted to the service of Dr. L. T. Barclay at the Toronto Western Hospital in 1939, complaining of increasing pain commencing two months previously in the proximal phalanx of the second toe. Later the toe became swollen. A radiograph (Fig. 16) shows marked bone condensation in the middle part of the diaphysis. Along the medial margin where condensation is greatest, there is slight periosteal, right angle new bone formation. Beneath this area in the deep margin of the cortex and bulging into the medulla there is the very faint outline of a dense rounded body partially surrounded by a very narrow radio-translucent ring. The neighbouring bones show considerable decalcification. The lesion was curetted in 1939 and microscopic sections of the tissue were sent to us by Dr. George Shanks. They show fragments of typical osteoid osteoma. Operation gave prompt relief from pain and on April 28, 1947, 8 years after operation, this man was reported well and free from symptoms.

CASE 12

A man of 30 years of age was admitted to another local hospital in March, 1933, complaining of severe pain in the arm and tenderness at a point corresponding to the tubercle of the radius. In 1930 he received a blow on the wrist following which he had intermittent pain from the hand to the elbow. At first mild, the pain gradually became worse and more frequent and finally constant and severe disturbing his sleep. External rotation of the forearm aggravated the pain. There was a mild tingling sensation in the hand and tenderness over the tubercle of the radius. In November, 1932, a radiograph was reported as negative. Five months later, March, 1933, a repeat radiograph (Fig. 17) revealed a radio-translucency of the tubercle of the radius extending up to the periosteum. There was no calcified core but in the lesion were fine linear radio-opaque streaks running at right angles to the surface. Osteogenic sarcoma was suspected. A hard, rounded body removed surgically was reported pathologically as osteogenic sarcoma. Disarticulation at the shoulder was advised but the patient refused this operation. A little later the upper one-third of the radius was resected. On review of the sections a few years later, the diagnosis was corrected to osteoid osteoma. This man is alive and well and has a good functioning arm 15 years after operation.

CASE 13

A boy of 18 years admitted to the Jewish General Hospital, Montreal, service of Dr. R. Breitman, on August 20, 1946, gave a history of pain in the left arm for about 1 year. For 1 month prior to admission the pain had been of a severe, stabbing character lasting about one minute and radiated down the arm and up into the neck and scapular region. Examination revealed a tender, hard mass about 2 inches long on the anterior surface of the humerus about its middle. There were no other significant signs or symptoms. Blood Wassermann was negative. A radiograph (Fig. 13) shows a circular translucent area in the cortex of the humerus. Close examination reveals a small central condensation largely obscured by the cortex. Overlying this defect and extending up and down the shaft for some distance, there is marked periosteal bone formation producing a thickening of the humerus cortex.

At operation on August 24, 1946, hard bone was chiselled away exposing what the surgeon thought was the medullary cavity obliterated by a mass of tissue the consistency of spongy bone. The surgical diagnosis was sclerosing osteomyelitis. It was obvious by a postoperative x-ray examination that the lesion was entirely within the cortex and that what the surgeon thought was medullary cavity was actually the osteoid nodule in the thickened cortex. The pathological diagnosis was osteoid osteoma. Following the operation relief of symptoms was prompt and the patient was free from symptoms 15 months later.

CASE 14

This young man of 21 years of age injured his left leg below the knee in 1945. There was pain and swelling of short duration. In August, 1946, he again sustained an injury to the same part, followed by a persistent, tender swelling and increasing pain in the upper leg, particularly severe on weight-bearing. On admission to the Montreal General Hospital on October 18, 1946, there were no other significant clinical findings. Radiographs showed marked cortical bone condensation and thickening posteriorly in the upper end of the tibia. Although no central rarefaction could be seen, an osteoid osteoma was suspected and the patient was brought back for further radiological examination. The second radiograph (Fig. 15) made with the Buckey diaphragm and more penetrating rays revealed in the centre of the condensed cortex very faintly, an oval, dense body surrounded by a narrow radio-translucent zone. This confirmed the suspicion of osteoid osteoma.

At operation on October 21, 1946, the thickened cortical bone was chiselled away. During this procedure a pea-sized brown firm nodule separated from the bone. The specimen received in the laboratory consisted of fragments of dense cortical bone measuring up to 2 cm. in thickness and a 5 mm. rounded, reddish brown nodule of bony consistency. The pathological diagnosis was osteoid osteoma and hyperplastic compact cortical bone. Relief of symptoms was prompt and a year later this man was free of symptoms.

CASE 15

An 11-year old girl entered the Jewish General Hospital, Montreal, service of Dr. Mark Kaufmann, on September 24, 1946, complaining of pain and swelling over the middle of the left tibia for three weeks. Her mother stated that the child had complained of pain in this location at intervals for the past year. Physical examination revealed over the middle third of the left tibia, a hard fusiform tender swelling. A radiograph showed cortical thickening of the antero-medial aspect of the middle third of the bone. In the centre of the condensed thickened cortex there was a faintly visible ring of rarefaction about a dense rounded body. The radiological diagnosis was sclerosing osteitis, osteoid osteoma or Ewing's tumour and a biopsy was advised. At operation on September 28, 1946, hard bone was chiselled away and underlying soft tissue was removed with a curette. No pus was encountered. The pathological diagnosis was osteoid osteoma. The patient was discharged, symptom-free and was still free of symptoms a year later.

THE PATHOLOGIC NATURE OF THE LESION AND ITS RADIOLOGIC APPEARANCES

It may be profitable to combine the discussion of the pathologic and radiologic findings in order that the interpretation of the latter may be based upon the former through the various phases of the development of this tumour. Early in the course of the disease, even though pain and tenderness and sometimes swelling of the soft tissues are marked, there may be no noticeable radiologic change whatever, as in case 12, or there may be general rarefaction of the bones

of the region without any localized demonstrable lesion as in cases 2 and 4. At this stage no one has had the opportunity of examining pathologically any of the bone tissue; therefore, the genesis of the lesion is not known. However, a very fair idea of it may be gained from a study of its later stages.

At a demonstrable stage the osteoid osteoma occurs as a more or less rounded nodule commonly 0.5 cm. and usually not exceeding 1 cm. in diameter. Occasionally it attains considerably larger dimensions as in case 4 in which the tumour measured 4.5 cm. in its longest axis. In location it may be entirely within cancellous bone, entirely within the cortex, subperiosteal, or in the deep margin of the cortex bulging into the medulla. Originating in the cancellous bone it may later involve the cortex. The consistency of the nodule varies from that of soft, spongy to hard bone. In colour it may be brownish red, pink or pearly gray.

In situ, demarcation of the nodule is sharp (Figs. 1 and 2). The cut surface on slight magnification is seen to be finely trabeculated (Fig. 3). Between the tumour nodule and the surrounding bone, a zone of loosely arranged cellular and vascularized connective tissue can be defined (Fig. 2). Higher magnification of this zone (Fig. 4) reveals that lacunar absorption and replacement of the pre-formed bone by this vascular actively growing connective tissue in which new bone may form, extends considerably beyond the actual tumour nodule. When the process reaches the periosteum that membrane is stimulated into active cellular proliferation followed by a new periosteal bone formation.

The little nodule can be easily separated from its bed through the zone of loosely arranged connective tissue immediately surrounding it. Hence, very commonly the specimen received in the laboratory consists of a small ball of tissue. The fundamental nature of this small ball, the osteoid osteoma, is that of a very cellular osteoblastic type of connective tissue, well vascularized and containing numbers of multinucleated giant cells (Fig. 5). It reminds one of the type of tissue seen in the metaphysis of the growing bone. It resembles somewhat the substance of the giant cell tumour and the intertrabecular tissue in active Paget's disease of bone. But in none of the specimens that we have examined has the content been entirely of this nature. If Fig. 5 is carefully examined, small, irregular, scattered deposits of osteoid can be detected. This illustration represents only a very small area of the tumour in Fig. 2. Elsewhere in that specimen well developed trabeculæ of osteoid are abundant. Fig. 6 taken from the tumour shown in Fig. 1 shows well developed, non-calcified osteoid trabeculæ. It is these trabeculæ that impart to the tumour its finely trabeculated appearance.

At this stage the radiograph will reveal a small more or less rounded radio-translucent area as in case 10, of three months' duration. The radio-translucent zone is comprised of the non-calcified tumour and the immediately surrounding zone of reactive connective tissue. Often at the periphery of the surrounding reactive connective tissue zone new bone formation may be stimulated and then a rim of bone condensation appears about the rarefied nodule (Fig. 8).

The next phase in the development of the tumour is calcification of the osteoid (Fig. 9). The time of its appearance is variable. It may take place almost as soon as the osteoid forms, yet it may be delayed for several months. Beyond the margin of the tumour nodule the vascular connective tissue zone described above persists. As time goes on, the cellular activity in the tumour diminishes, giant cells become fewer and vascularity lessens and layers of calcifying osteoid may be deposited upon the original calcified trabeculæ forming atypical irregularly lamellated bone (Fig. 10). The radiographic appearance now will be that of the previous stage described above but, in addition, there will be in the radio-translucent zone a central opaque body which will vary in size and density according to the extent and degree of calcification of the osteoid. The non-opaque rim about the dense nodule can be accounted for by the reactive connective tissue about the tumour and by non-calcified tissue at the periphery of the tumour. When the lesion is located in cancellous bone it stands out distinctly in the radiograph as a small dense body surrounded by a zone of radio-translucency (Figs. 11 and 12). This is a very common and characteristic radiologic appearance of the osteoid osteoma and is often seen on first examination of the patient.

When the tumour is located in the cortex, or involves it from the medulla, the proliferative cellular reaction about the tumour may be at-

tended by an increased bone formation in the cortex and in the overlying activated periosteum resulting in a more or less marked cortical thickening and condensation. This reaction may extend a considerable distance beyond the tumour, as illustrated in Figs. 12 to 16. So dense may be this bone reaction that, by the ordinary radiologic technique, the embedded tumour is scarcely visible (Figs. 13 and 16) or it may be entirely obscured and the use of the Buckey diaphragm and more penetrating rays will be required to visualize it as in case 11 (Fig. 15). It is to be noted that the calcification of the tumour does not bear any direct relation to the degree of surrounding proliferative bone reaction. The radiographic appearance of the condensed central core in the tumour may or may not exist in the presence of a marked surrounding bone reaction.

As previously mentioned the osteoid osteoma may be located subperiosteally. Jaffe in one of his papers presents a very good example. In our own material case 12 showed a rather unusual appearance. The lesion was located in the tubercle of the radius. The radiograph (Fig. 17) shows an oval radio-translucent area from which a similar translucent tract extends through the cortex to the surface. In this tract faint condensed streaks can be seen at right angles to the surface. It was probably this appearance that raised the suspicion of sarcoma which was at first mistakenly confirmed on biopsy, but later corrected to osteoid osteoma.

In this lesion of osteoid osteoma there appears to be two distinct features. One is the circumscribed nodule forming the tumour; the other is the surrounding zone of proliferating connective tissue. This connective tissue may do one of two things, or both. It may and probably always does cause lacunar absorption of preformed bone and then later provides the connective tissue bed for additional bone formation in membrane, thus accounting for the condensation and thickening of the bone about the tumour. Just what the relationship is between the tumour and the surrounding reactive process is difficult to explain. That the reactive process is dependent upon the tumour is borne out by the fact that removal of the tumour brings about a cessation of the reactive process and eventual restitution of bone architecture, as illustrated by case 1. Furthermore if, in the course of operation, the tumour is not removed symptoms and the progress of the lesion continue.

The evolution of the osteoid osteoma is, like other benign tumours of bone, a relatively slow process. The initiation of the tumour we may presume to be a proliferation of the intertrabecular bone-forming mesenchyme which by its pressure effects, causes bone pain. It is attended by a vascular disturbance manifested by swelling of the soft tissues. This phase may continue for some time without showing any focal bone replacement noticeable in the radiographs. There may however be some general rarefaction of the bone of the region due to the local vascular disturbance and disuse because of pain. This phase may persist for at least seven months as in case 2, but usually is of much shorter duration. It is followed by local bone absorption due to the lytic action of the tumour and the lesion then becomes demonstrable radiologically as an area of radio-translucency. Later a central condensed core appears when the osteoid becomes calcified. The surrounding proliferative cellular reaction, particularly when the cortex and periosteum become involved, provokes new bone formation which may extend far beyond the tumour and may be so dense, as seen in the radiograph, as to entirely mask the appearance of the little tumour.

Knowing the behaviour of this peculiar lesion, two important procedures can be recommended in those cases in which the characteristic appearance of the tumour is not noticed radiologically.

1. In those cases in which the symptoms of troublesome pain, tenderness, soreness or stiffness, and often swelling suggestive of osteoid osteoma are present and the first radiologic examination reveals no lesion or only general rarefaction of the bones of the area, further exposures should be made at various angles and should be very carefully examined because the focal radio-translucency may be very faint or masked by the accompanying surrounding bone rarefaction. If by this means demonstration of the lesion fails, repeated radiographs should be made at short intervals until a diagnosis can be made.

2. In the presence of suggestive symptoms when only marked eccentric cortical condensation and thickening can be demonstrated by the usual radiologic technique, further examination by the use of the Buckey diaphragm and more penetrating rays should be carried out in an effort to demonstrate the embedded little tumour.

CLINICAL CONSIDERATIONS

The osteoid osteoma is a disease affecting chiefly young adults and adolescents and occurs about twice as often in the male as in the female. In this series of cases, the ages ranged between 11 and 36, with one at 44 years. It has been reported as early as 1½ years and as late as 49 years. Ten cases were males and five, females.

The skeletal location is predominantly in the bones of the lower limbs which were involved in 10 of the cases. Three were in the upper limbs, 1 in the mandible and 1 in the transverse process of a vertebra. As yet this tumour has not been reported in the ribs, clavicles, scapulæ or skull bones other than the mandible. There is no good reason to believe that it should not appear in these bones.

Pain is the outstanding symptom. It was because of this that all but one of the cases sought medical attention. At first intermittent and mild, it increases in severity and persistence and may be troublesome enough to interfere with sleep. Active movements and weight-bearing may aggravate it. Usually it is localized to the area involved, but it may radiate for some distance as in cases 9, 12 and 13. However, pain is not always complained of, nor is it always severe. In case 8 there was none. In cases 3 and 10 the complaint was of soreness rather than definite pain. In case 7 symptoms followed a fall on the knee 24 hours previous to the finding of a well developed osteoid osteoma in the patella and could not therefore be attributed to the tumour. Tenderness over the location of the tumour is a pretty constant sign. In several cases it was not mentioned, but in only one was it said definitely that there was none.

Swelling of the regional soft tissues is often found and in those cases where the cortex is involved, the underlying hard cortical swelling can be palpated. Limitation of joint movements seems to be due to the pain evoked and stiffness is probably due to the soft tissue swelling. Local heat and redness is persistently absent.

Trauma cannot be considered an etiologic factor. In only 4 cases was trauma referred to by the patients as a cause of their trouble. In one it antedated symptoms by 4 months. In another, a blow on the wrist appeared to initiate symptoms which were promptly relieved three years later by removal of an osteoid osteoma in the upper end of the radius. In the third case symptoms followed immediately after trauma to the part and two months later a well developed osteoid osteoma accompanied by a marked and wide area of cortical thickening was demonstrated, a lesion much larger than would be expected at two months. In the fourth case pain and tenderness followed a fall on the knee 24 hours prior to the finding of a well developed osteoid osteoma in the patella. It appears that trauma may initiate symptoms in the presence of an already developing tumour.

There is usually no significant rise in temperature, pulse rate or leucocytes and regional lymph nodes rarely enlarge. In case 4 in which there was an unusually large and active tumour in the os calcis and into which there was hæmorrhage, there was slight elevation of temperature and a palpable catarrhal inguinal lymphadenopathy.

TREATMENT

Surgical removal of the tumour gave prompt relief from symptoms and a lasting cure in 11 cases. In 8 of these the tumour was removed by the chisel and curette. Two amputations and one resection, done under mistaken diagnoses, also gave prompt and lasting cures. Two were not operated on and have been lost track of. One recent case, advised to have the tumour removed, has not yet been operated on. Another one in which symptoms were slight has been advised against operation and has improved under treatment by active exercises. The outcome of this last case will be watched with interest. Judging by the behaviour of the other cases and those reported by other authors, we would not be surprised if the return and increase of symptoms necessitated the removal of the tumour.

It is interesting to speculate as to what might be the fate of this tumour if left untreated. Cases with troublesome symptoms come to operation. But what happens in those cases in which symptoms are mild or absent? It is not inconceivable that the ossified tumour might fuse with the surrounding condensed bone, accounting for some of those foci of osteopetrosis accidentally found in the bones on radiologic examination.

SUMMARY

Fifteen cases of osteoid osteoma are reported. The pathology of the lesion in its various phases is discussed in correlation with the radiologic

findings. The clinical features and results of treatment are also discussed.

We are indebted to our pathologist colleagues, Dr. Morris Simon of the Jewish General Hospital, Montreal, and Dr. N. Sharp of the Toronto Western Hospital and to the radiologists of those two hospitals for permission to use their materials. We appreciate very much the kindness of the surgeons mentioned for allowing us to make use of their cases.

REFERENCES

1. JAFFE, H. L.: *Arch. Surg.*, **31**: 709, 1935.
2. JAFFE, H. L. AND LICHTENSTEIN, L.: *J. Bone & Joint Surg.*, **22**: 645, 1940.
3. JAFFE, H. L.: *Radiology*, **45**: 319, 1945.
4. BERGSTRAND, H.: *Acta Radiol.*, **11**: 597, 1930.
5. HITZROT, J. M.: *Ann. Surg.*, **91**: 450, 1930.
6. JAFFE, H. L. AND MAYER, L.: *Arch. Surg.*, **24**: 550, 1932.
7. HEINE, J.: *Arch. f. Klin. Chir.*, **146**: 737, 1927.
8. OTTOLENGHI, C. E.: *Bol. y trab., Acad. Argent. de Chir.*, **24**: 553, 1940.
9. BADO, J. F. AND LARGHERO, I. P.: *Rev. brasil. de orthop. y traumatol.*, **2**: 139, 1941.
10. Case records Massachusetts General Hospital, case No. 27492, *New England Med. J.*, **225**: 920, 1941.
11. HORWITZ, T.: *Radiology*, **39**: 226, 1942.
12. BARRON, L. J.: *Bull. Hosp. Joint Dis.*, **3**: 141, 1942.
13. KLEINBERG, S.: *New York State J. Med.*, **43**: 332, 1943.
14. STAUFFER, H. M.: *Am. J. Roentgenol.*, **52**: 200, 1944.
15. LEWIS, R. W.: *Am. J. Roentgenol.*, **52**: 70, 1944.
16. HAMILTON, J. F.: *Surg. Gyn. & Obst.*, **81**: 465, 1945.
17. Case records Massachusetts General Hospital, case No. 31432, *New England Med J.*, **233**: 508, 1945.
18. VOSTREL, A. F. AND APPLEBY, G. S.: *Bull. School Med., University Maryland*, **30**: 140, 1946.
19. CAMPOS, A. P.: *J. Internat. Coll. Surg.*, **9**: 112, 1946.
20. WEIDIN, W. M. AND OLIVA, J. J.: *Am. J. Surg.*, **71**: 558, 1946.
21. *New England J. Med.*, **233**: 601, 1945.

B.C.G. VACCINE IN THE PREVENTION OF TUBERCULOSIS

B. McKone, M.D.

London, Ont.

B.C.G. (bacillus of Calmette and Guerin) vaccine consists of a one time virulent strain of bovine tubercle bacilli. After years of subculturing and experimenting with animals, Calmette and Guerin discovered that the organism gradually became innocuous for all laboratory animals. Since its first trial on humans in 1921 (by Weill-Hallé, Paris) considerable controversial articles and papers appeared in the literature. (By 1934, 1,600 papers had been written on the subject[3]). Finally, after 25 years the use of the vaccine is becoming increasingly more popular throughout the world.

Reaction of host to B.C.G. vaccine.—Rosenthal[1] demonstrated by animal inoculation (guinea pigs) that the organisms could be given intradermally, intravenously, intracardially, intraperitoneally and intratesticularly in large quantities without producing progressive tuberculosis. In another experiment he describes the development of tubercles, and finally their complete resolution, following guinea pig inoculation with 10 to 15 mgm. of the organisms intracardially.[2] All cells (due to tissue response) disappeared by the end of the third month. Fibrosis or caseation rarely occurred and restitution was complete. Kayne[3] mentions the work of K. A. Jensen (Holland) in which the protective mechanism in vaccinated guinea pigs is a delaying of the effect of virulent bacilli on this highly susceptible animal.

Harmlessness of B.C.G. for humans.—Kayne[3] again, quotes Irvine (1934),

> "If we review the whole of this chapter we see a great tragedy in Germany, (Luebeck disaster) due to a contaminated vaccine, a suspicious but inadequately investigated minor disaster in Hungary, a doubtful incident in Chile, and several suggestive but quite unproved individual cases (of tuberculosis developing following B.C.G. but not proved due to B.C.G.). When we consider that 1,343,000 infants have been given the vaccine and there is not yet one sure case of death from the B.C.G., we should indeed be cautious if we still doubted the safety of the vaccine for normal infants. Even if every case (of tuberculosis) mentioned in this chapter had been proved to be due to the B.C.G., the ratio to the total number inoculated would only have been just under 1 in every 15,000."

From 1934 and to this day, to the best of my knowledge there are no reports of any ill effects following vaccination with B.C.G. vaccine. Heimbeck of Norway, Wallgren of Sweden, Baudóuin of Montreal, Ferguson of Saskatchewan, Aronson and Danenberg of Philadelphia, Kereszturi and Park, New York City, Rosenthal of Chicago make no mention of ill effects in over 30,000 infants, children and adults vaccinated since 1934.

Birkhaug of Norway stated at the N.T.A. meeting, Buffalo, N.Y., June, 1946, that tuberculin negative student nurses and applicants for medical schools are accepted for training only if rendered positive following B.C.G. vaccination. Ferguson, Saskatchewan, at the same meeting stated that tuberculin negative reactors working in a sanatorium environment, provided they are rendered positive to old tuberculin following vaccination, are now granted insurance as arranged by the Saskatchewan Tuberculosis League.

Results of vaccination in humans.—Heimbeck[4] (Norway) in a study among student nurses from 1927 to 1938 at the Ullevaal Hospital, Oslo, presented the following results. Among previously positive reacting student nurses, without history or evidence of disease on commencing training, 3.29% developed tuberculosis but there were no deaths. Among those negative reactors not receiving the vaccine 34.15% developed tuberculosis and 4.23% of the total

negative reactors died. Among the positive reactors, rendered positive following vaccination, 3.52% developed tuberculosis and there were no deaths.

R. G. Ferguson[5] in a study from 1934 to 1943 among nurses in general hospitals and sanatoria in Saskatchewan showed a definite reduction in morbidity rate to at least its fourth. Because of his results the C.T.A. has adopted the use of B.C.G. vaccine, at present, particularly for those living or working in a tuberculous environment. (C.T.A. Conference, Quebec City, May, 1947.)

Methods of vaccination.—B.C.G. vaccine was first given (1921) orally to infants on the 5th, 7th and 9th days of life. This is still being carried on today in 3 doses of 10 mgm. by weight of the organisms in 2 c.c. sterile saline. Heimbeck in 1926 introduced the subcutaneous route, while Wallgren of Sweden in 1927 the intradermal route; each using 1 to 2 mgm. in 1/10 c.c. saline. In 1939, Rosenthal introduced the multiple-puncture method, and Weill-Hallé the scarification method, both using concentrated vaccine. Ferguson, in his study, used the intradermal route, the dosage being 0.5 mgm. in 1/10 c.c. in two areas about 1" apart. The multiple-puncture method developed by Rosenthal[6] will probably become the most widely used. It consists of placing a drop of B.C.G. vaccine on the outer aspect of the alcohol-cleansed arm, through which 30 punctures are executed over an area of 2 x 2.5 cm. This method has produced tuberculinization in 99.4% of the vaccinated within a period of a month.

The writer's method of the vaccination was the intradermal injection of 1/25 mgm. as recommended by Dr. Armand Frappier in a personal communication to the late Dr. C. H. Playfair, in 1946. It would appear, however that the important factor is to obtain a definite positive tuberculin reaction to 1 mgm. O.T. in 2 to 3 weeks following vaccination. There does not appear to be any severe reaction to this higher concentration if positive results are shown. The scratch and puncture methods give a higher percentage of positive reaction in 2 weeks than the other methods, nevertheless Dr. Ferguson's method has been suggested as a standard.

Duration of allergy.—It is obviously difficult to determine duration of allergy to old tuberculin B.C.G. vaccination. However, a study was made by Debre and Cofino in France between 1922 and 1926. They reported on 132 vaccinated and 141 unvaccinated infants who were placed in a healthy environment. At the age of 4 years 88.6% of the vaccinated group were still positive reactors, whereas all of the non-vaccinated group were still negative reactors.

Reaction of vaccination.—From personal observations of approximately 75 persons vaccinated ranging from 16 to 40 years (1 girl 9 years), using intradermal and scratch method, no general reactions have occurred. Regional adenitis as yet has not been observed. Local reaction following the intradermal route ranges from a small red area of induration to an area 1 cm. in diameter of redness, induration and sero-pustular formation. The pustule is small and is seldom tender. The few on whom this occurred had no complaints, but were naturally curious. The final picture is a pin-head-sized scar. The induration may last 6 to 12 weeks, and few of the pustules lasted more than 6 to 9 weeks. The scarification method, although only about 15 have been observed by the writer, presented redness and some induration only, for 3 to 6 weeks. In the first 30 vaccinated (intradermally with 1/25 mgm.) by the writer only 92% were positive in 6 weeks. At that time the vaccinated were tested on the 3rd and 6th week following vaccination with 1/10 mgm. O.T. followed by a second test of 1 mgm. O.T. on the 6th week. Only 10% required the 1 mgm. dose of O.T.; 67% were positive to 1/10 mgm. in 3 weeks.

Selection of candidates for vaccination. — Those persons whose Mantoux test is definitely negative to 1/10 mgm. O.T. on the 48 hour reading are given 1 mgm. 1/100 O.T. immediately. If their reaction using fresh dilutions of O.T. is still negative, (particularly in the younger age group) it is considered that they have never had a tuberculous infection. In the case of infants or children recently exposed to a tuberculous infection, it is suggested that an interval of 2 to 3 months be allowed to elapse after separation from the source, for the final tests prior to vaccination.

Retesting following vaccination. — It is suggested that between 3 and 4 weeks following vaccination 1 mgm. 1/100 O.T. be given. This can be done safely and is time saving. If nega-

tive, the test could be repeated in 6 to 8 weeks and if still no reaction occurs, the vaccination can be repeated. It has often been recommended that persons planning on working in an infectious environment be rendered positive prior to commencing such work. This is considered important for the protection of the present reputation of B.C.G. as a valuable weapon in the fight against tuberculosis.

DISCUSSION

Many factors are important in considering the use of B.C.G. vaccine. Every effort should be made to avoid indiscriminate use of the vaccine, since the method of vaccination is inexpensive and would appeal to the public generally. Little would be gained, and much of the present public health prevention and control measures might be lost. The preparation of the vaccine should be limited to the well established laboratories already supplying it, for use in man. A seminar on B.C.G.[7] in June, 1947 (U.S.A.) presented many interesting facts. The following are statements of the moderator, H. C. Sweany, at the beginning and conclusion of the meeting.

"Certain facts have been learned: It has been proved beyond doubt that B.C.G. is harmless, that it is feasible to administer the vaccine to human beings, and that it offers some degree of protection against a later infection with virulent tubercle bacilli. The unfavourable features are the dangers of contamination or mixing cultures with virulent strains, the difficulty of applying it to great masses of people, the false security that may be engendered by its use, and that it does not afford the complete protection that smallpox vaccination does. It seems clear that, if rigidly supervised, B.C.G. has a place in anti-tuberculosis work."

SUMMARY AND CONCLUSIONS

1. B.C.G. vaccine is innocuous and is of definite value in the prevention of tuberculosis.

2. It is recommended for use among those negative reactors destined to live or work in a tuberculous or potentially tuberculous environment. Infants and children whose parents or other members of the family are stricken with the disease; our young women planning or already training as nurses; and any group working in a sanatorium environment, are among those recommended for vaccination.

REFERENCES

1. ROSENTHAL, S. R.: *Arch. Path.*, **22**: 348, 1936.
2. *Idem*: *Am. J. Dis. Child.*, **54**: 296, 1937.
3. KAYNE, G. G.: *Am. Rev. Tuberc.*, **34**: 10, 1936.
4. HANSEN, O. G.: *Tubercle*, **25**: 1, 1944.
5. FERGUSON, R. G.: *Am. Rev. Tuberc.*, **54**: 325, 1946.
6. ROSENTHAL, S. R.: *Am. Rev. Tuberc.*, **57**: 110, 1948.
7. Moderator, Seminar on B.C.G.: *Am. Rev. Tuberc.*, **57**: 95 and 113, 1948.

RÉSUMÉ

Description du B.C.G. et des réactions qui suivent son emploi, chez l'animal et chez l'homme. Discussion des résultats obtenus et exposé des diverses méthodes de vaccination. La méthode intradermique paraît la plus simple mais il semble que la méthode par scarification sera la plus employée. Le B.C.G. est inoffensif et les résultats obtenus à la suite de son emploi sont indéniables. On l'emploiera chez les individus Mantoux-négatifs qui doivent séjourner où il y a des tuberculeux, notamment chez les infirmières; chez ceux qui vivent dans les sanatoria et auprès de tuberculeux.

JEAN SAUCIER

INFECTIOUS POLYNEURITIS OF UNKNOWN ETIOLOGY (Guillain-Barré Syndrome) IN CHILDHOOD

Jorge E. Howard, M.D.*

Santiago, Chile

and

Valerie Friedman, M.D., C.M.

The Children's Memorial Hospital, Montreal, Que.

THE polyneuritides have for several decades been described under many headings.† In 1916, Guillain, Barré and Strohl[1] separated from the polyradicular neuritides, a group of patients who had, besides the symptoms common to polyneuritis, an increase in the cerebrospinal fluid proteins but without cellular reaction. In subsequent years more of these cases were recognized and many case reports and excellent monographs on this condition appeared in the literature, stressing the more important findings and adding new ones.[2, 3]

For more than 20 years all the cases reported were in adults; indeed it was considered a disease of adult life until Ford[4] and Hecht[5] in 1937 reported cases in children. Hecht described 7 cases of "acute infective polyneuritis" in children between the ages of 2 and 10 years, which illustrate the clinical picture. In 1941, Casamajor and Alpert[6] reviewed the English and French literature and found 38 cases reported in children under 12 years of age. They described three additional cases bringing the total to 41. Since then several reports have appeared

* Resident in Medicine.

† Such as infective polyneuritis, acute febrile polyneuritis, Landry's ascending paralysis, polyradiculoneuritis, polyneuritis, acute infectious neuronitis, Guillain-Barré syndrome, Guillain-Barré-Strohl syndrome, radiculoneuritis and polyneuritis of unknown etiology.

commenting on the relative frequency and importance of this condition in childhood.[7, 8]

The etiology of this disease still remains obscure. It is the modern consensus that the disease is caused by a neurotropic virus closely related to that of poliomyelitis. Some authors have even considered this condition an abortive form of poliomyelitis but no proof in support of this view has been advanced. Attempts to reproduce the disease in mice, guinea pigs, rabbits and monkeys have been unsuccessful.[9]

Lewey,[10] in 1945, studied the histopathological changes in 2 specimens of sacral roots and found an almost identical picture in both, a "peracute radiculopathy". Macroscopically, there is always œdema of the brain, spinal cord and peripheral nerves, with congestion of the meninges. Microscopically, the peripheral nerves show œdema, infiltration of inflammatory cells and vascular congestion of the bundles. There is swelling of the myelin sheathes and fragmentation of the axis cylinders. The anterior horn cells also show changes, principally chromatolysis and vacuolization. The changes are most marked in the peripheral and cranial nerves but it is of interest to note that all the changes are reversible. Post-mortem examinations have revealed that the disease affects the viscera but clinically no systemic manifestations are found.[9]

Although the etiology of this syndrome is not known and the pathological lesions are not characteristic, it is interesting that the clinical picture is so well defined. Generally, there is a history of a slight upper respiratory infection 8 to 10 days prior to the onset of symptoms. The mildness of these preceding infections makes it difficult to evaluate the real rôle played by them in the general picture of this syndrome. Shortly after the onset of these mild symptoms, signs of peripheral neuritis develop symmetrically in the lower extremities and muscle tenderness may be noted as well as sensory changes. All patients later develop a symmetrical flaccid paralysis of the lower extremities. In some patients the paralysis continues to advance upward and may result in a complete quadriplegia. The rate of spread, as well as the degree of involvement, is quite varied; the paresis may be only manifested by awkwardness in the performance of voluntary movements, while in others it may be complete. There is no special wasting or atrophy of muscle groups other than that referable to disuse. At other times the sensory symptoms may be the first to appear. When they do occur they are generally limited to the distal portions of the extremities. The other neurologial manifestations that have been described in this condition are not characteristic. Cranial nerve involvement is seen frequently.[11, 12] Ford and Walsh[13] reported a case with increased cranial pressure and papillœdema.

The findings in the cerebrospinal fluid are of great importance in this condition. The most characteristic change is the so-called albuminocytological dissociation, that is, an elevation in the protein content without a cellular increase. In 1936, Guillain[14] postulated that a protein level of over 300 mgm. % was an essential finding for the diagnosis. This figure is definitely too high, since typical cases have been reported with protein values close to 100 mgm. %. In some instances the increase in proteins does not occur at the onset of the motor changes but appears later in the course of the disease.[15] The rest of the cerebrospinal fluid findings are generally normal, although xanthochromia may at times be found.

The most important point in differential diagnosis is to separate it from acute anterior poliomyelitis, and because of the different prognosis the establishment of the correct diagnosis is of more than academic interest. The important points to consider in differentiating these two conditions are: the seasonal epidemic incidence of poliomyelitis, the absence of fever or of constitutional signs at the onset of the motor disturbances and the marked symmetry of the lesions in the Guillain-Barré syndrome. If albumino-cytologic dissociation is present, this is in favour of the latter, although it is sometimes seen in poliomyelitis.[17, 18, 19] Again, if the recovery is complete, without muscular atrophy or contractures, the diagnosis of Guillain-Barré syndrome would appear more logical. We have seen several borderline cases in which accurate diagnosis was impossible, and until further knowledge of the etiology of the Guillain-Barré syndrome is achieved, they will remain unclassifiable. The second important differential diagnosis that should be considered is lead poisoning, but x-ray, hæmatological and clinical studies should simplify the differentiation. The other polyneuritides, such as those due to diphtheria, syphilis or vitamin B deficiency, usually offer little difficulty in the differential diagnosis, but when doubt persists, laboratory examinations

are of aid. In the early phase of the neurological form of acute porphyria the symptoms may simulate a Guillain-Barré syndrome, and differentiation here is aided by spectrographic studies and the fact that the urine when exposed to light, darkens. Pseudo-hypertrophic muscular dystrophy at its onset may also simulate the Guillain-Barré syndrome.

The prognosis of this condition in childhood is good, as compared to an approximate 20% mortality in adults.[16] The duration of the symptoms is quite variable and they may last from 2 weeks to 2 to 3 years. Recovery of function follows in reverse order in which they were lost. One of the main purposes of this report is to present the case histories of 4 children with Guillain-Barré syndrome. We present our histories in detail so that comparison with the disease in the adult may more easily be made. We feel that the group, though small, gives the average picture of the disease in children.

CASE 1

J.J., a 5-year old boy, was admitted to the Children's Memorial Hospital on May 17, 1941, with the chief complaint of inability to walk for 2 days. His past history was irrelevant. He was in apparent good health 9 days prior to admission when he developed a slight cold with a low-grade fever which lasted for 1 day. He was not kept in bed. Three days before admission to hospital, his mother noticed that he did not want to play and that he had some difficulty in walking, stumbling and falling several times. The following day he complained of a slight pain in his arms and back, appeared listless and refused his meals. He was then admitted to hospital.

Examination revealed a well developed, well nourished child, in no acute distress. He was afebrile, a little drowsy and somewhat irritable. He could stand up, but on attempting to walk, after the first step or two, would fall. There was indefinite weakness of arms and legs which appeared to be more marked in the proximal segments. Straight arm and leg raising from the prone position were adequately performed but not maintained for any length of time. Ankle, knee and radial reflexes could not be elicited. The remaining reflexes were normal and there was no cranial nerve involvement. There was slight tenderness in the popliteal spaces but no definite joint or muscle tenderness. Sensory responses to touch, pin prick and position were also normal. White blood count showed a leukocytosis of 13,000 cells with a slight neutrophilia. Repeated urinalyses were normal. Blood Wassermann and Mantoux of 0.1 mgm. O.T. were negative. Throat culture showed a slight growth of *M. catarrhalis*. X-ray studies of the long bones showed no lesion. On the day following admission lumbar puncture revealed a crystal clear fluid, with an initial pressure of 130 mm. of water. On microscopic examination 4 cells per c.mm. were found. The biochemical examination revealed: proteins 175 mgm. %, chloride 435 mgm. %, glucose 68 mgm. %.

He was given 5 mgm. of thiamine chloride by mouth daily from the time of admission. During the first week he became progressively weaker. A second lumbar tap on the 5th hospital day showed an increase in the cerebrospinal fluid proteins to 230 mgm. % with only 3 cells. During the second hospital week the child became progressively weaker and was unable to lift his arms or raise his head without assistance. He also complained of pain behind both knees. By the third hospital week he had begun to improve and could hold his arms up while the muscular tenderness was less marked and his general disposition was excellent. A third lumbar puncture on the 23rd hospital day showed a mildly positive Pandy reaction and no cells. At this time the route of administration of the thiamine chloride was changed to daily intramuscular injections. He improved rapidly, and was discharged from hospital 6 weeks after admission with nearly normal muscular power. He was followed by the Physiotherapy Department and discharged as cured on August 15, 3 months after admission to the hospital.

CASE 2

M.N., a 2½-year old boy, was admitted to the Children's Memorial Hospital on April 4, 1944, with the complaints of refusing to sit, stand or walk for the last 3 days. Past history was irrelevant.

The child was well until approximately 10 days prior to admission, when the parents noted that he was holding himself very stiffly, and had some difficulty on micturition accompanied by dysuria, voiding only once a day. He was seen at that time by his family physician who advised circumcision. Two days before admission he refused to sit or stand and appeared to have pain when his legs were touched. He did not seem ill and his temperature was normal, but as these symptoms continued, he was brought to the hospital.

Examination showed a pale, well developed and well nourished child who was fretful and unco-operative, preferring to lie on his side. He would not sit or stand. There was no frank paralysis and he could move his legs somewhat, especially to withdraw them from painful stimuli. Power in the upper extremities was better. When he cried, the umbilicus moved upward suggesting relative weakness of the recti below the umbilical level. Ankle and knee reflexes could not be obtained, radial reflexes were greatly diminished. Response to painful stimuli was fair, there was no cranial nerve involvement and the fundi were normal. Hæmoglobin, white blood count and differential showed normal values for his age. Mantoux 0.1 mgm. O.T. and blood Wassermann were negative. Throat culture showed a slight growth of a hæmolytic streptococcus. Urinalysis and x-ray studies of the long bones were normal. Lumbar puncture on the day of admission revealed a slightly xanthochromic fluid with a few crenated red blood cells, 3 lymphocytes per c.mm., a positive Pandy reaction and on biochemical examination a protein level of 251 mgm. %.

In the hospital, the general weakness became more marked, he could not withdraw his legs to painful stimuli and weakness of the depressors of the lower lip, especially on the right, was noticed. There was no hyperæsthesia on stroking the leg, but the calf muscles were tender on pressure and passive movements of the legs became very painful. He became incontinent of both urine and fæces. On admission because of pain, he was started on a daily intramuscular injection of 25 mgm. of thiamine chloride. The pain disappeared after 10 days of therapy.

A second lumbar puncture done on the 12th hospital day revealed a very faintly xanthochromic fluid with a protein content of 420 mgm. % and no cells. At this time his general picture was the same, with the exception that the superficial reflexes were now very difficult to elicit. On the 20th hospital day he developed measles and was transferred to the isolation pavilion. Following this episode, he began to recover gradually and 5 weeks after admission he was able to sit up in bed. He continued to progress favourably and 11 weeks after admission was discharged from the hospital. He was followed by the Physiotherapy Department and 5 months after the onset of symptoms was discharged with normal muscular power.

CASE 3

P.S., a 2-year old girl, was admitted to the Children's Memorial Hospital for the first time on April 17, 1946. Her past history was irrelevant. One month prior to admission it was noted that she sat and stood up with

difficulty. This weakness increased steadily and 2 weeks before admission she began to complain of abdominal pain and of pain in her knees. One week before admission she began to have difficulty in swallowing and her voice became hoarse.

Physical examination showed a well developed, well nourished child, lying comfortably on her back. During examination she became fretful, cried with a weak voice, and it was noticed that she had a somewhat nasal quality to her speech. She refused to walk or stand up. She could maintain the sitting position, but trunk and neck muscles were obviously weak as she could easily be tipped off balance. Arms and legs were generally weak but there was no gross wasting. The soft palate moved poorly but she appeared to swallow without regurgitation, although choking and coughing after swallowing. No deep reflexes could be obtained, and no pain or gross loss of pain sensation were noticed. The white blood count was 10,000 with a normal differential count; hæmoglobin was 10.6 gm. %. Repeated urinalyses were normal. Mantoux 0.1 mgm. O.T. and blood Wassermann were negative. A throat culture revealed no pathogenic organisms. X-rays of the skull, chest and long bones were essentially normal. A lumbar puncture done the day after admission showed a slightly xanthochromic fluid with 16 cells per c.mm., a positive Pandy reaction and a protein content of 435 mgm. %. At this time, daily intramuscular injections of thiamine chloride, 20 mgm., were instituted.

Eight days after admission a 2nd lumbar puncture resulted in clear fluid with 10 cells, a positive Pandy reaction, and on chemical analysis, proteins 221 mgm. %, sugar 97 mgm. % and chloride 446 mgm. %. Two weeks after admission, her weakness became very marked and tenderness, mainly distal to the knees, was elicited. This marked weakness lasted for a period of 5 to 8 days when a remarkable improvement was noted. One month after admission, the greater part of the motor function of her lower extremities had returned and 5 weeks after admission she was able to walk unaided. During her 6th week in the hospital, she developed scarlet fever and was moved to the isolation hospital. At this time examination showed absent knee reflexes and a slight weakness of both lower extremities. On discharge from the isolation hospital, 2 weeks later, her recovery was complete.

CASE 4

S.M., a 10½-year old boy was admitted to the Children's Memorial Hospital on May 29, 1946, with complaints of difficulty in standing up and in walking for 10 days prior to admission and pain in the thighs for 2 days at the onset of symptoms. His past history was irrelevant.

He was in apparent good health until 12 days before admission when he awoke complaining of pain in his thighs and calves. These pains persisted for 2 days and were relieved by massage. Ten days prior to admission, while walking, he fell several times and his parents noted that he walked in a very "disjointed" manner. This progressed until he was unable to walk.

Examination showed a well developed, well nourished boy, lying comfortably in bed in no apparent distress. Temperature, pulse and respirations were normal. General physical examination was essentially normal, positive objective findings being limited to the neurological examination. There was no pain or muscle tenderness. He had marked symmetrical weakness of all muscles of the lower extremities. On standing he was very unstable and he was unable to rise on his toes. There seemed to be slight weakness of the biceps, triceps and handgrip. There was some difficulty in sitting up or turning over, indicating some trunk involvement. No facial or bulbar involvement was present, and respiratory movements were normal. All deep reflexes were abolished. Sensation and superficial reflexes were normal. White blood count was 7,800, with a normal differential. Urinalyses were normal. Mantoux test with 0.1 mgm. O.T. and blood Wassermann were negative. Several throat cultures revealed non-pathogenic organisms. X-rays of the long bones were normal. Lumbar puncture the day after admission revealed a xanthochromic fluid under normal pressure. On microscopical examination no cells could be seen, and the chemical analysis showed an elevated protein content of 221 mgm. %. Daily intramuscular injections of 20 mgm. of thiamine chloride were instituted.

During the first month of hospitalization there was a marked progression of the weakness, the lower extremities became completely paralyzed and he lost about 75% power of the upper extremities. He could not hold his arms in the outstretched position and could not lift his head off the pillow. However, he could turn his head and elevate his shoulders well, indicating good function of the sternocleidomastoids and the trapezii. Intercostal movements were good, but his cough was feeble, indicating some weakness of the respiratory muscles. No cranial nerve involvement was noted. Complete areflexia persisted. Cerebrospinal fluid protein was still very elevated. (For details of spinal fluid see Table I.) By the middle of July, 2 months after the onset of symptoms, he showed wasting of the extremities, and despite a rigid regimen of physiotherapy, contractures of the hands were developing.

TABLE I.

	Cells	*Colour*	*Protein mgm. %*	*Chloride mgm. %*	*Glucose mgm. %*
May 30	0	xanthrochromic	221		
June 21	2	clear	220	436	91
Aug. 6	0	xanthrochromic	650	443	
Aug. 20	0	xanthrochromic	424	412	91
Sept. 21	1	xanthrochromic	142	439	84
Dec. 11	0	xanthrochromic	50	415	67
Feb. 15	0	clear	30	415	70

Ten weeks after admission active movements of the upper extremities were first noted, he stated he felt better and his apathy disappeared. He then slowly and gradually began to improve. Four months after admission he began to have movements in his lower extremities and the contractures of the hands were disappearing. At this time a bilateral foot drop was noted. Coincidental with his clinical improvement a decrease in the cerebrospinal fluid proteins was noted. Six months after admission he began to walk unaided although his gait was far from normal. He continued to progress and at present, 1 year after onset of illness, his muscular power is normal.

DISCUSSION

Although the Guillain-Barré syndrome is not common in childhood, we have encountered 4 typical cases in the past 5 years. During the same period this general pædiatric hospital had a total of 19,560 admissions, giving a ratio of 1 to approximately 5,000 admissions. We have also had the opportunity of studying 5 other patients, who, although they had a peripheral neuritis and showed various other features of the Guillain-Barré syndrome, failed to present the complete association of symptoms necessary to this diagnosis. The exact nature of these 5 cases, which we have not included, has not been definitely established, and it is possible that these represent atypical forms of the syndrome.

From the study of these cases, the following differential points may be considered in com-

parison with cases described in adults. Apparently there is wide variation in age, the youngest of our series being 2 years, the oldest 10½ years of age. The onset is generally quite rapid. In 3 of our patients the exact moment of appearance of the symptoms could be determined, *viz.*, 3, 10 and 12 days before admission. One child, case 3, had a long prodromal period of approximately 1 month, simulating the onset as seen in the adult.

The most frequent complaint was difficulty in walking, which was a major feature in our 4 cases. The preponderance of the motor signs over the sensory was striking in all cases. In fact, in 2 patients (3 and 4), no changes in sensation could be elicited, and only 1 patient (2) were they of such degree as to make the child uncomfortable. The three youngest patients in our series appeared quite contented and even euphoric, while the oldest (4) showed the apathy usually seen in adult patients with this condition. Susman and Maddox[20] also commented on the apparent euphoria of these children which, we think, could be in part explained by the absence of pain.

Among adults, 35 to 50% of all cases show some involvement of cranial nerves, particularly of the 7th or facial nerve. The only evidence of facial nerve involvement among our cases was in patient No. 2 who showed a transient weakness of the depressors of the lower lip. In patient No. 3, cranial nerve involvement was manifested by difficulty in swallowing and by a hoarse voice with a distinct nasal quality. A notable feature of our series was the complete absence of respiratory involvement. It is well known that the prognosis in childhood is almost uniformly excellent, as contrasted with the mortality of approximately 20% found in adults. Since the deaths among adult patients are, for the most part, secondary to a paralysis of the respiratory muscles, the sparing of these muscles in children is probably the major factor in the usually favourable outcome. In all 4 patients of our series, recovery was complete.

As in adults, the course of this disease in childhood is variable. Our case 1 is an example of a short course. This 2½ year old child showed complete recovery after only 2 months. In contrast with this, in case 4, the child began to show signs of recovery only after 11 weeks and was not considered cured until 1 year after onset.

Throughout our series, we obtained the impression of a correlation between clinical and biochemical findings. This was shown most strikingly by patient No. 4 (see Table I), in whom a definite clinical improvement was found to coincide with a definite decrease in cerebrospinal fluid proteins.

Since this syndrome tends to be self-limited and in children eventual complete recovery is the general rule, it is difficult to estimate the efficacy of the various treatments that have been proposed. There is no specific treatment beyond symptomatic relief and general nursing care. During the convalescent stage, physiotherapy in the form of hydrotherapy, massage and exercise, has proved of benefit. The use of thiamine chloride intramuscularly in large doses has been reported as beneficial in relieving the sensory symptoms; as in children the sensory symptoms are of secondary importance we may argue that its routine use is probably unwarranted. This argument is supported by our own experience in these 4 cases. The Kenney method too has been used, but without particular success.[24] More recently Shaeffer[22] and Test[23] have reported on the use of neostigmine methyl sulphate and in their cases the authors thought it contributed greatly to the rapidity of the patient's recovery. We have had no experience with either of these last methods.

SUMMARY

Four case histories of the Guillain-Barré syndrome in childhood have been presented. They illustrate the differential features of the disease in children in comparison with the disease in the adult, namely, the wide range of age, rapid onset, great preponderance of motor signs over sensory symptoms, the variable course and the good prognosis. In this small series a suggested impression of some correlation between clinical and biochemical findings has been obtained.

REFERENCES

1. GUILLAIN, G., BARRÉ, J. A. AND STROHL, A.: *Bull. et soc. méd. d'hôp. de Paris*, 40: 1462, 1916.
2. BRADFORD, J. P., BASHFORD, E. F. AND WILSON, J. A.: *Quart. J. Med.*, 12: 88, 1918.
3. CASAMAJOR, L.: *Arch. Neurol. & Psychiat.*, 2: 605, 1919.
4. FORD, F.: Diseases of the Nervous System in Infancy, Childhood and Adolescence, Chas. C. Thomas, 1937.
5. HECHT, M. S.: *J. Pædiat.*, 11: 743, 1937.
6. CASAMAJOR, L. AND ALPERT, G. R.: *Am. J. Dis. Child.*, 61: 99, 1941.
7. HATOFF, A.: *J. Pædiat.*, 24: 393, 1944.
8. GILLESPIE, J. B. AND FIELD, E. H.: *J. Pædiat.*, 14: 363, 1939.
9. SABIN, A. B. AND AZING, C. D.: *Am. J. Pathol.*, 17: 469, 1941.
10. LEWEY, F. H.: *J. Pædiat.*, 26: 165, 1945.
11. VIETS, H. R.: *Arch. Neurol. & Psych.*, 17: 794, 1927.
12. PULLEN, R. L. AND SODEMAN, W. A.: *Am. J. M. Sc.*, 211: 110, 1946.

13. FORD, F. R. AND WALSH, F. B.: *Bull. Johns Hopkins Hosp.*, **73**: 391, 1943.
14. GUILLAIN, G.: *Arch. Neurol. & Psych.*, **36**: 975, 1936.
15. STONE, T. T. AND ALDRICH, K.: *J. Am. M. Ass.*, **114**: 2196, 1940.
16. FOX, M. J. AND O'CONNOR, R. D.: *Arch. Int. Med.*, **69**: 59, 1942.
17. JERVIS, G. A. AND STRASSBURGER, P. J.: *Am. J. Dis. Child.*, **65**: 431, 1943.
18. NICHOLSON, J. H.: *New England J. Med.*, 235: 214, 1946.
19. DE SANETIS, A. J. AND GREEN, M.: *J. Am. M. Ass.*, **118**: 1145, 1942.
20. SUSMAN, E. AND MADDOX, K.: *Med. J. Australia*, **1**: 158, 1940.
21. ROSEMAN, E. AND ARING, C. D.: *Medicine*, **20**: 463, 1941.
22. SHAFFER, J. O.: *J. Am. M. Ass.*, **131**: 285, 1946.
23. TEST, C. E.: *J. Am. M. Ass.*, **132**: 1070, 1946.
24. ARING, C. D. AND SABIN, A. B.: *Arch. Neurol. & Psych.*, **47**: 938, 1942.

STRICTURES OF THE COMMON DUCT*

Warren H. Cole, M.D.

Chicago, Ill.

THE treatment of strictures of the common bile duct has always been complicated, and followed by results which are relatively poor, except that during the past few years results have improved. It is true that with almost any type of repair, results will be good for a short time, up to one or two years following repair. Because of this tendency for the stricture to reform, decision cannot be made regarding the final result until two or two and a half years have elapsed since repair. This feature has been one of the factors in the confusion in following the results in various types of operations.

ETIOLOGY OF STRICTURES OF THE COMMON DUCT

During the past 11 years (1936-1947), we have encountered 39 patients with stricture of the common duct at Illinois Research and Educational Hospital. The relative incidence of causative factors in this group is shown in Table I.

TABLE I.
INITIAL CAUSE OF BENIGN STRICTURE
(In our series of 39 patients)

Cause of stricture	*No. of cases*	*Percentage*
Operative trauma	25	64
Inflammation	8	20
Chronic fibrosing pancreatitis	5	13
Pancreatic cyst	1	3
Total	39	100

N.B. Only 3 patients, excluding the pancreatic group, were jaundiced before cholecystectomy.

(From Cole, Reynolds and Ireneus in *Advances in Surgery*, Interscience Publishers, Inc., N.Y., 1948).

*From the Department of Surgery, University of Illinois College of Medicine, and the Research and Educational Hospital, Chicago, Ill.

Numerous mechanisms may produce strictures of the common duct (see Fig. 1). Unfortunately, carelessness, haste, and inadequate knowledge of anatomy (including particularly the anomalies) are responsible for most of the strictures produced by operative trauma. Too commonly, serious hæmorrhage from the cystic artery is allowed to develop, and is stopped by blind stabbing with an artery forceps which may have included part of the common duct, with damage of that structure by the ligatures controlling the bleeding point. Occasionally a stricture is produced by the scarring resulting from the healing of an ulceration in the wall of the duct produced by a gallstone. Very rarely indeed does a stricture result from the trauma or effect of choledochostomy.

PREVENTION OF STRICTURES

Since the operative treatment of the common duct is so difficult and so commonly followed

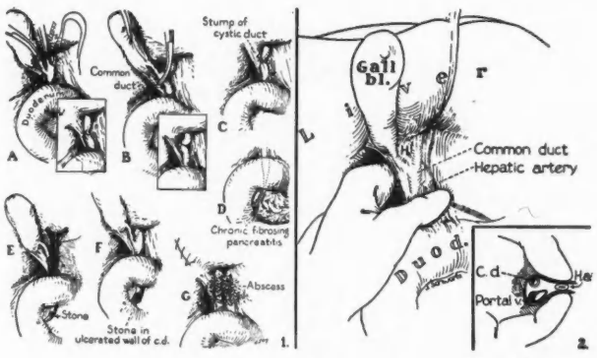


Fig. 1.—Mechanisms in production of stricture of the common duct; (A) transfixion with a needle; (B) ligation with the cystic; (C) ligation of the cystic duct too close to the common; (D) diffuse sclerosing pancreatitis; (E) cholangitis; (F) ulceration of the wall by stone; (G) abscess or local collection of bile. (From Cole, Ireneus and Reynolds, in Strictures of the Common Duct, Interscience Publishing Co., New York, 1948). **Fig. 2.**—Control of hæmorrhage by insertion of the index finger in the Foramen of Winslow and compression of the hepatic artery between the index finger and thumb. (From Cole, in Operative Surgery, D. Appleton-Century Co., New York. In press).

by poor results, it is obvious that great attention must be paid to prevention of strictures. Careful observance of the precautions listed below will minimize stricture formation.

1. *Obtain good exposure.*—Since it is so essential to see and identify structures during operations on the biliary tract, the incision must be made long enough to obtain good exposure and retraction must otherwise be effective. Good anæsthesia with proper relaxation is essential in biliary surgery.

2. *Isolate the junction of the common duct before ligating the cystic.*—Since adhesions are usually present in this area it is essential to carry out good dissection of the cystic duct and a segment of the common duct adjacent so that trauma to the latter structure may be avoided.

3. *Ligate the cystic duct and artery separately.*—By this process the surgeon will minimize the possibility of ligating a portion of the common duct in the large mass which presumably contains the cystic duct and artery.

4. *Cut no structure until identified.*—This rule should always be respected regardless of the accuracy of the surgeon's knowledge of anatomy, because anomalies are so common.

5. *Ligate no artery until it is proved the vessel enters the gall-bladder.*—Observance of this rule will eliminate the occasional error of ligature of the right hepatic artery for the cystic.

6. *Avoid blind stabbing with an artery forceps to control hæmorrhage.*—When a hæmorrhage develops in the depths of the wound around the common duct, the surgeon must at all times retain his composure and insert his finger into the foramen of Winslow which will then allow him to compress the hepatic artery between index finger and thumb (see Fig. 2). When the hæmorrhage is controlled by this method the surgeon can easily find the bleeding point by gradually releasing the vessel to find the source of hæmorrhage.

7. *Start dissection of the gallbladder at the fundus when adhesions are dense around the common duct.*—Brief exploration by the surgeon will readily reveal how much difficulty is apt to be encountered in isolating the various anatomical structures around the common duct; if adhesions are so dense that dissection will obviously be difficult. If adhesions are dense, it is much safer to start dissection of the gallbladder from the bed of the liver at the fundus. By this method, the gallbladder itself can be isolated more safely although the bleeding will be greater following this method than when dissection is started from the cystic duct upward.

The surgeon must be thoroughly acquainted with the anatomy of the structures in the operative field and must likewise be familiar with the numerous anomalies which can be present. Since anomalies are so common in this area, the fact that the surgeon is very familiar with anatomy does not eliminate the necessity of paying strict attention to the precautions previously described.

DIAGNOSIS OF STRICTURE OF THE COMMON DUCT

When the common duct is completely blocked jaundice will develop in 48 to 72 hours unless a fistula forms with subsequent loss of bile to the exterior. Development of a fistula or jaundice within a few days following operation on the biliary tract should make the surgeon suspicious of a mechanical obstruction to the common duct. One must bear in mind, however, that occasionally jaundice is produced by a hæmatoma or bile in the peritoneal cavity. More accurate evidence of obstruction to the common duct will be examination of the stool for bile.

The important symptoms of stricture of the common duct are jaundice, pain, pruritus, chills, fever and acholic stools. If the jaundice develops several weeks or months after an operation on the biliary tract, lesions other than stricture of the common duct must be considered. The amount of pain produced by stricture is usually insignificant, although it may be fairly pronounced during the first two or three days following an acute block; it usually diminishes to an insignificant degree thereafter. When the obstruction develops slowly, pain will usually be absent, although when a suppurative cholangitis develops (as is indicated by the presence of chills and fever), there may be a moderate amount of pain in the epigastrium. During the formative stage of stricture of the common duct the stools will be intermittently cholic and acholic. After the stricture has completely formed the stools will remain acholic, although there will frequently be a slightly yellow tinge to the stool because of excretion of bile pigment through the mucosa of the intestine.

Previous history will be of great value in aiding in differentiation, particularly since operative trauma is such a common cause of stricture. In the absence of previous operation on the biliary tract, the diagnosis of stricture, therefore, becomes less likely. Under such circumstances, stone in the common duct, carcinoma of the pancreas or ampulla of Vater become likely possibilities. As a matter of fact, a stone in the common duct is a strong possibility even though the patient has had a

previous operation for gallbladder trouble. This is particularly true if the patient had symptoms of stones in the common duct, and no stones were removed from the common duct at the previous operation. If the obstruction is due to stone, there will invariably be much more pain than when the symptoms are caused by stricture. The surgeon must bear in mind, however, that after the first few days pain may be very trivial in obstruction due to stone. Although carcinoma of the pancreas is less apt to produce pain in the epigastrium, it must be remembered that in fully 20% of cases pain may be a serious complaint.

If there has been a history of pancreatitis, the surgeon must bear in mind the possibility of pancreatitis involving the head of the pancreas, or diffuse sclerosing pancreatitis, if the symptoms include jaundice. Rarely is jaundice produced by the usual type of acute œdematous pancreatitis or acute hæmorrhagic pancreatitis except for slight icterus in the latter type. A blood amylase test will aid considerably in differentiation since an obstruction of the common duct proximal to the pancreas will not be associated with an elevation of blood amylase. If the obstruction is produced by a lesion in the pancreas, whether by localized pancreatitis, or diffuse fibrosing pancreatitis, an elevated blood amylase will be noted in 30 to 40% of cases.

PREOPERATIVE CARE

Patients with stricture of the common duct rapidly become afflicted with numerous nutritional deficiencies and imbalances. Almost all of them lose weight due to lack of appetite and disturbance in digestion. The presence of bile in the gastro-intestinal tract is an important factor in proper utilization of food and in maintenance of appetite. With few exceptions, hypoproteinæmia and anæmia develop sooner or later. All of the symptoms just mentioned are aggravated if infection (*i.e.*, suppurative cholangitis) develops. Of the various organs damaged by the stricture and its consequence, the liver is probably the most important. Hepatic insufficiency is observed fairly consistently in all the patients, and it is usually explained on the basis of diminished glycogen content, infection and biliary stasis (unless a fistula is present).

In view of the deficiencies mentioned above, it is essential that very effective preoperative care be instituted. The patient should be encouraged to eat food which he likes and which has maximum food value. It is usually advisable to supplement oral intake with intravenous glucose and small quantities of intravenous amino acids. Blood and plasma are administered depending upon the levels of the blood protein and red blood cell count. If a biliary fistula is present fluid and electrolyte imbalances are apt to develop, particularly in warm weather. Clinical examination of the patient and laboratory data including particularly the plasma chloride levels will determine the amount of fluid and electrolytes needed.

TECHNIQUE OF REPAIR OF STRICTURES

As in the operative treatment of many other conditions, no one type of operation can be applied to all of the various types of stricture encountered. The surgeon must be familiar with numerous procedures and likewise be familiar with indications for the various operations.

Regardless of which of the various methods described herein is utilized in the repair, the *exposure of the hilus* of the liver and the ends of the duct represent one of the most difficult parts of the operation. After the abdominal cavity has been opened it is usually preferable to start dissection alongside the liver, approaching the region of the hilus from the anterolateral direction. The adhesions will invariably be so dense that sharp dissection is required. If sharp dissection is carried downward too rapidly and carelessly, the portal vein or hepatic artery may be opened. This is particularly true if the common duct is entirely missing. If the common duct is present it will be encountered and opened before either of the two vessels just mentioned are injured. When the region of the hilus is approached, exploration of the area with a syringe and needle is necessary to identify structures and find the proximal end of the common duct. Finding the distal end of the common duct is usually more difficult than finding the proximal, particularly if a large portion of the duct has been obliterated by the so-called obliterative cholangitis, or has been removed at a previous operation. Careful search should be made for the distal end since the sphincter of

Oddi is such an important structure which cannot be duplicated by the ingenuity of man. Cattell[4] has emphasized the advisability of completely mobilizing the duodenum and head of the pancreas, and splitting the head of the pancreas to find the distal end of the duct. With this mobilization, it will usually be possible to anastomose the two ends of the duct together.

1. *Repair of local stricture.*—When the stricture involves only a very short portion of the common duct the operation is much easier than in strictures of other types, and is associated with better results. Ordinarily, the stenosed area can be freed from adjacent tissues, the stricture resected, and end-to-end anastomosis performed. Some type of support is needed at the suture line to prevent reformation of the stricture. Perhaps the best method of obtaining this support is to insert a T-tube proximal or distal to the suture line so that an arm of the T-tube projects past the line of anastomosis. It is essential that this T-tube not be brought out through the suture line. This tube should be left in place for at least three months.

2. *Anastomosis of side of common duct to duodenum.*—Two methods of performing anastomosis of this type are available. In one method, the stoma is made by a transverse incision in the common duct and a longitudinal incision in the duodenum. Interrupted catgut is used for the inside row and interrupted silk or cotton for the outside layer. If the lumen appears to be small, a short piece of a rubber catheter may be inserted before the inside row of sutures is completed. The catheter extends from the common duct down into the duodenum and allows free flow of bile into the duodenum which might be prevented by œdema if no support were used. Such a catheter will remain in place only 10 or 15 days. In another method emphasized by Sanders,[5] the duodenum is mobilized sufficiently to allow it to be brought alongside the common duct, and the stoma made by longitudinal incision in both structures with sutures as described above.

3. *Anastomosis of the hilar duct to a loop of jejunum.*—A few years ago we performed 5 such operations, bringing a loop of jejunum up toward the hilus of the liver where it was anastomosed to the stump of the common hepatic duct. An entero-enterostomy was performed between the two arms of jejunum, hoping to prevent regurgitation of food up around the loop into the intra-hepatic bile ducts. We found, however, that although we performed an anastomosis between these two arms of jejunum with a long stoma, food continued to go around the loop. Results were very poor in this group primarily because of suppurative cholangitis which we proved in two of the 5 cases to be due to regurgitation of food and secretion into the intrahepatic bile ducts. We have abandoned this type of operation.

4. *Anastomosis of the hilar duct to a Roux Y arm of jejunum.*—I am convinced that the utilization of the Roux Y arm represents a definite improvement in the repair of strictures of the common duct. Three methods of repair are available. With either method the formation of

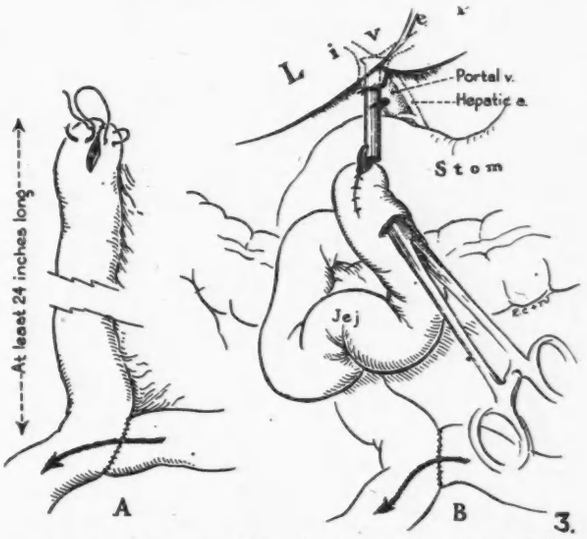


Fig. 3.—After the ileum is severed and the proximal end sutured to the distal loop at least 18 inches from the point of severance, the distal end is closed with a continuous suture as shown in (A). The end of the vitallium tube is inserted into the end of the intestine, aided by a hæmostat through a puncture wound two or three inches from the closed end as shown in (B). (From Cole, Ireneus and Reynolds, in *Annals of Surgery*, 1945).

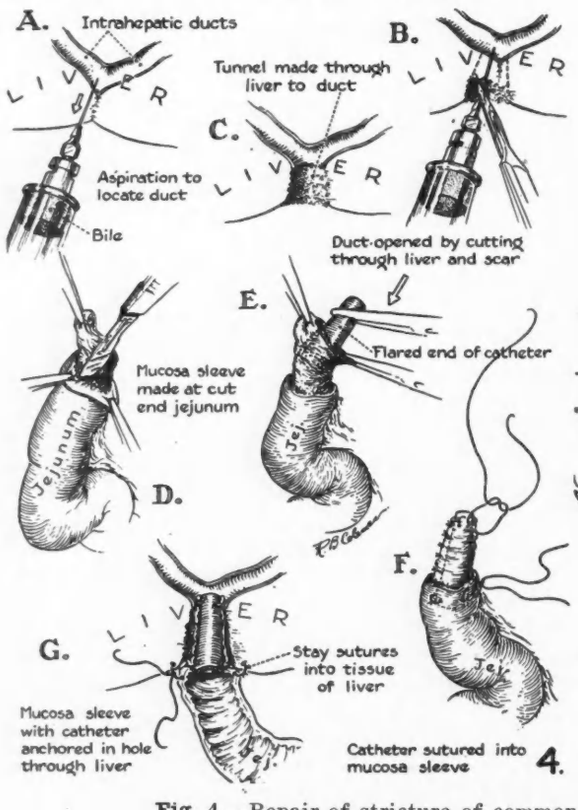
the Roux Y arm of jejunum is the same. The jejunum is transected about 18 inches from the ligament of Treitz, and the proximal end anastomosed to the distal about 18 inches from the point of section. Anastomosis at this point may be performed by a lateral, or by an end-to-side anastomosis. The free arm of jejunum is brought upward toward the liver anterior to the colon if the mesentery is long enough to permit it. If the mesentery is short the arm of jejunum is brought up through a hole in the mesocolon taking care later to anchor the edge of the opening thoroughly to the arm of jejunum so

that loops of intestine will not herniate through the opening.

A. *Utilization of a vitallium tube.*—Since the introduction of the vitallium tube by Pearse[6] several years ago in the repair of strictures of the common duct, it has been used by numerous surgeons. Some surgeons have abandoned its use because of the frequency with which the tube plugs and drops out of position. Other surgeons have had better luck with the tube and still utilize it. There are several methods of anchoring it in place. The author prefers to insert the bell end of the tube into the stump of the hilar duct anchoring it in place with a purse-string suture of silk or cotton (see Fig. 3). The end of the arm of jejunum is closed except for a central portion allowing protrusion of the tube into the lumen of the jejunum. It is usually preferable to insert a long clamp through a hole in the end of the jejunum (as illustrated in Fig. 3), and grasp the end of the tube to be certain it protrudes into the lumen of the jejunum. The serosal margin of the end of the jejunum is then anchored to the hilus of the liver. Omentum should be placed around the operative site, but a Penrose drain must be inserted down to the suture line and kept in position for at least six or seven days. Recently, we have been anastomosing the two ends together in an end-to-end fashion on the assumption that recurrence of stricture will be minimized.

B. *Utilization of a catheter.*—Allen[8] has recommended insertion of the bell end of a rubber catheter up into the biliary duct, threading it into the end of a Roux Y arm of jejunum and out through an opening in the wall of the intestine. The end of the jejunum is turned in with formation of a cuff and this cuff sutured to the hilus of the liver to prevent leakage. An opening is made in the wall of the catheter which is contained in the intestine so that bile can flow from the liver into the intestine, or from the liver through the catheter to the exterior.

C. *Use of mucosal graft (modification of Hoag operation).*—Several years ago Hoag[9] introduced anastomosis of the end of the hilar duct to the mucosa of the stomach, hoping to minimize stricture formation. I am convinced that this procedure has definite merit and with my associates I have modified the procedure with utilization of the end of the Roux Y arm of jejunum. It appears that this procedure would be particularly indicated when no stump of duct is available and when scarred liver tissue must be incised or excised to gain access to the duct. I am convinced that stricture formation is greatest on the liver side of the anastomosis. Therefore, if an epithelial graft can be utilized (see Fig. 4) stricture formation might be minimized. A tube of mucosa can be obtained readily by separating the mucosa and submucosa from the muscularis by sharp dissection. The epithelial tube stretches out and becomes quite thin allowing it to be inserted around a rubber tube through a relatively small opening up to the stump of the common hepatic duct. The rubber tube and its surrounding mucosal graft is pushed up into the opening and anchored in place by two or three interrupted sutures. The supporting tube consisted of a bell end of a catheter of appropriate size. After insertion of sutures to hold the mucosal tube in place, the wound is closed around a drain as in other operations.



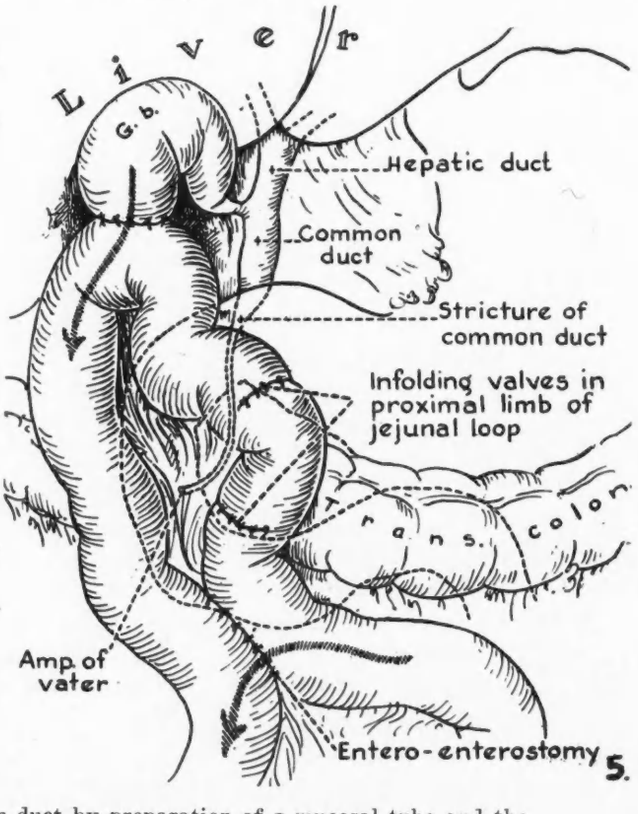


Fig. 4.—Repair of stricture of common duct by preparation of a mucosal tube and the implantation in the duct at the hilus of the liver. This procedure is most applicable when no stump of duct remains, and scarred liver tissue must be incised to reach the duct. The depth of the scarred area is rarely as pronounced as illustrated. (Modification of Hoag operation). **Fig. 5.**—Use of defunctionalized loop of jejunum in re-establishment of bile flow in presence of obstruction of the common duct. An entero-enterostomy is performed between the two arms of jejunum and 2 or 3 folds placed in the proximal arm to prevent regurgitation. This operation is most applicable when obstruction is temporary as in obstruction due to pancreatitis, but may be used in any stricture if the gall-bladder is present, and the junction of the cystic and common ducts is proximal to the obstruction. (After Peterson and Cole, in *Archives of Surgery*, 1948).

5. *Anastomosis of the gallbladder to a loop of jejunum.*—When the gallbladder is present, as may occur in stricture due to diffuse sclerosing pancreatitis and carcinoma of the pancreas, it may be used in establishing a passageway for bile into the intestine if the gallbladder is not too badly diseased. In the traditional operation the gallbladder was anastomosed to the duodenum. However, anastomosis of the gallbladder to a loop of jejunum is preferable except when early demise is expected. The author prefers to perform an entero-enterostomy between the two arms to prevent regurgitation of food and intestinal secretions into the duodenum (see Fig. 5). However, unless the loop of jejunum is defunctionalized by placement of 2 or 3 folds in the proximal arm (Peterson and Cole[10]) food will continue to pass through the entire loop even though an enter-enterostomy is made between the two arms of jejunum. Observation by x-ray for 2 or 3 hours following oral administration of barium will prove this point. The anastomosis between the gallbladder and jejunum is best made by utilizing interrupted fine catgut for the inside layer and interrupted silk or cotton for the outside layer. In reality, a Roux Y arm of jejunum is preferable to this defunctionalized loop, but the latter is less difficult and more rapidly performed.

TABLE II.

SUMMARY OF RESULTS IN REPAIR OF STRICTURES
(53 operations in 39 patients)

Type of operation	*No. of operations*	*Results (Except operative deaths)*	*Operative deaths*
Hilar duct to Roux Y (80% vitallium tubes)	22	82% good to excellent 18% failure	0
Hilar duct to mucosal flap jejunum (modified Hoag operation)	4	75% good to excellent 25% failure	0
Repair local stricture	4	66% good to excellent 33% failure	1
Hilar duct to duodenum	7	10% excellent 30% fair 60% failure	0
Miscellaneous types of operation	16	54% good to excellent 46% failure	3
Summary	53		4

Operative mortality rate 7.5%

RESULTS

In 53 operations for stricture of the common duct[11] we had 4 deaths, constituting a mortality rate of 7.5%. Walters[12] reports a mortality rate of 10% in 98 cases, and Cattell[4] 13.8% in 123 cases. Since nutritional deficiencies are so common in these patients, thorough preoperative preparation cannot be emphasized too much. Table II illustrates the symptomatic results in patients encountered in our series. The best results were obtained when we anastomosed the hilar duct to a Roux Y arm of jejunum. On most occasions a vitallium tube was used to support the anastomotic line in this series of operations. However, we feel that utilization of the mucosal flap of jejunum (modification of the Hoag operation) will actually yield better results. Our experience with this operation (4 cases) is too limited to arrive at any definite conclusions.

If the two ends of the duct can be approximated, an end-to-end anastomosis over a T-tube or vitallium tube should yield the best results. Cattell[4] is so convinced of the superiority of the end-to-end approximation that he actually advises splitting the head of the pancreas in an effort to find the distal end of the common duct. He reports the use of a vitallium tube as a support of the suture line in 23 patients having end-to-end repair. In this series 90% are listed as having satisfactory results. In this type of repair when end-to-end anastomosis can be achieved, we prefer to use a T-tube if there is room to bring it out through an opening separate from the line of anastomosis.

In a recent summary of results of numerous surgeons throughout the country following the use of vitallium tubes, Pearse[13] reports that good results were obtained in 80.1% in 106 collected cases. Obstruction due to blocking of the tube was noted in 11.3% of his combined series. In 79 patients a vitallium tube was used to support the anastomotic line between the hilar duct and duodenum; good results were obtained in only 58.2% of this group. We agree with the conclusions derived from these figures, namely that vitallium tubes should not be used to support the suture line

between the hilar duct and the duodenum. We have abandoned the old, traditional operation in which the hilar duct is anastomosed to the duodenum. In a small series of 7 patients in whom we performed this operation, we had a recurrence of the stricture in 57%.

Some surgeons anastomose the hilar duct to a loop of jejunum, and perform an entero-enterostomy between the two arms of jejunum. In our early experience in repair of stricture of the common duct we utilized this procedure, but had such poor results that we abandoned it. We are convinced that regurgitation is a major factor in these poor results, because two of our patients who had chills and fever due to suppurative cholangitis were relieved completely and promptly of their symptoms when we interrupted the proximal arm, thus preventing regurgitation of food and intestinal contents into the intrahepatic ducts. When we utilize anastomosis of the bile duct or gall-bladder to a loop of jejunum we always make folds in the proximal loop to prevent regurgitation. However, in our estimation the use of the Roux Y arm is more effective in preventing this regurgitation.

REFERENCES

1. GRAHAM, R.: Personal communication.
2. FLINT, E. R.: *Brit. J. Surg.*, **10**: 509, 1923.
3. EISENDRATH, D. N.: *J. Am. M. Ass.*, **71**: 864, 1918; *Med. & Surg. J.*, **182**: 573, 1920; *Surg., Gyn. & Obst.*, **21**: 1, 1920.
4. CATTELL, R. B.: *Surg. Clin. N. Am.*, **23**: 701, 1943; *J. Am. M. Ass.*, **134**: 235, 1947; personal communication.
5. SANDERS, R. L.: *Ann. Surg.*, **123**: 847, 1946.
6. PEARSE, H. E.: *Surgery*, **10**: 37, 1941.
7. COLE, W. H., IRENEUS, C. AND REYNOLDS, J. T.: *Ann. Surg.*, **122**: 490, 1945.
8. ALLEN, A. W.: *Ann. Surg.*, **121**: 412, 1945; personal communication.
9. HOAG, C. L.: *Surg., Gyn. & Obst.*, **64**: 1051, 1937.
10. PETERSON, L. W. AND COLE, W. H.: *Arch. Surg.*, In press.
11. COLE, W. H., REYNOLDS, J. T. AND IRENEUS, C.: Advances in Surgery, Interscience Publishing Co., New York. In press.
12. WALTERS, W.: *J. Am. M. Ass.*, **113**: 209, 1939.
13. PEARCE, H. E.: *Ann. Surg.*, **124**: 1020, 1946.

RÉSUMÉ

La cause la plus fréquente des rétrécissements du cholédoque est le traumatisme opératoire. L'inflammation, beaucoup moins fréquente, doit également être retenue. On évitera les rétrécissements du cholédoque par une bonne dissection de la région, isolant parfaitement les divers canalicules et vaisseaux et en ne se servant de la pince hémostatique qu'à bon escient. Le diagnostic sera posé après enquête anamnestique complète: opération antérieure sur les voies biliaires, recherche de néoplasmes pancréatiques ou ampullaires, calculs, pancréatite. Les soins préopératoires sont très importants et il faudra relever le bilan nutritif de ces malades. Plusieurs opérations sont discutées mais la meilleure semble être l'anastomose du canal hilaire au jéjunum selon l'Y de Roux, avec ou sans tube de vitallium. Le tube de vitallium a ses partisans et ses antagonistes. L'abouchement du canal hilaire au duodénum est abandonné. La technique recommandée est celle qui expose le moins aux régurgitations.

JEAN SAUCIER

THE ROLE OF SURGERY IN MYASTHENIA GRAVIS*

W. Carleton Whiteside, M.D., F.R.C.S.[C.], F.A.C.S. and Carman Weder, M.D.†

Edmonton, Alta.

THE thymus, albeit an organ of much dispute and conflicting views as to its essential nature and function, is, as a study of its morphology shows, legitimately to be included in consideration of both the hæmatopoietic system and the glands of internal secretion.

We desire to confine this presentation of the rôle of surgery in myasthenia gravis to its relation with the thymus gland and to present two cases treated beneficially by surgery for this disease.

The anatomical details of the thymus are quite well established. It may be mentioned however that it may be variable in its position and has been located posterior to the innominate vein. It is important not to mistake this anomaly for an absence or atrophy of the thymus. The thymus gland rapidly shrinks in disease and starvation and hence is seldom observed in its true light regarding its size. The recent war proved conclusively that, in the wounded or killed, the thymus weighed on the average of 30 grams. Also shown by Hammar some years ago in a series of accident cases which expired, he found the largest in adults to be 37.5 grams and 15 grams in middle life.

Much work has been done on the physiology of the thymus and the conclusions would appear to be that the gland plays a part with the glands of internal secretion, for its removal from the chain causes definite changes in the osseous and sex characteristics, whereas Rowntree's intraperitoneal injections of thymic extract showed a profound effect in the rate of development and precocity. In the physio-pathology of the thymus in myasthenia gravis, it is the opinion of McEachern and many other observers that the substance acetylcholine is produced in the neighbourhood of the junction between the motor nerve ending and the muscle fibre. When the nerve is stimulated a minute quantity of acetyl-

* Read before the Annual Meeting of the Royal College of Physicians and Surgeons of Canada, November, 1947. For lack of space some abbreviation of this paper has been necessary.

† House-surgeon, University of Alberta Hospital.

choline is released and this chemical (or electrical) charge somehow activates the muscle. Limitation of its action is determined by the presence in both the blood stream and tissues of another substance, cholinesterase, an enzyme which destroys excess of acetylcholine.

The balance of these reactions results in the normal function of voluntary muscle. The poison, curare, which produces a paralysis of voluntary muscle is believed to act by interfering with the response of the muscle fibre to the chemical (or electrical) stimulus. This finding was first noted by Dr. Margaret Walker of England. The state of a patient with myasthenia gravis is very much like curare poisoning and the facts are best fitted by the supposition that the circulation of such a person has a substance which tends to inhibit the production of acetylcholine and that a dysfunction of the thymus produces this substance just as one finds in toxic goitre, adrenal tumours, adenomas of the pancreas, each of which produces changes in the bio-chemical and physiological set up. It has been more recently shown by Wilson and Stoner that serum in the case of myasthenia gravis when injected into the peritoneal cavity of animals causes an interference in the muscle nerve preparation. Trethewie and Wright of Australia obtained similar results in humans.

It would then appear that myasthenia gravis is not a disease of the nervous or muscular system but a biochemical one and dependent upon the endocrine organs. Since the effect is generalized its agent must be carried by the blood stream.

PATHOLOGY OF THE THYMUS GLAND

The lesions of the thymus may be considered under the following headings:

1. *Hypoplasia.*—(*a*) The normal process of partial involution already alluded to. (*b*) Premature, a pathological involution, even a complete atrophy of the gland, may be observed at an early age in a number of chronic infectious and wasting conditions, such as infantile marasmus, tuberculosis or starvation.

2. *Hyperplasia.* — (*a*) Primary, apparently forming part of the clinical syndrome known as status thymo-lymphaticus. (*b*) Secondary. A simple active proliferation of the thymus is known to occur in association with a number of glandular and other diseases, such as Graves' disease, Addison's, acromegaly and myasthenia gravis.

3. *Vascular changes and inflammation.*—(*a*) Acute congestion of the thymus, sometimes with hæmorrhage into the gland, is found in a number of acute infections as in bronchopneumonia, rarely in tuberculosis and syphilis. (*b*) Leukæmia and lymphosarcoma may have an association with the thymus.

4. *Tumours.* — Primary tumours are more frequent than formerly realized. The majority of thymic neoplasms show evidence of malignancy. (*a*) Innocent tumours include lipomata, fibromata, dermoid cysts and simple cysts. (*b*) Malignant tumours. There is much debate between the various observers as to the nomenclature to be adopted in these tumours. Maximov in 1931 classified these as follows: (1) Spindle-celled sarcoma, from the capsule and interlobular connective tissue, many of these are now classed as in the following. (2) Carcinoma, arising from the reticulum cells and Hassall's corpuscles. (3) Lymphosarcoma, arising from the lymphocytes.

E. T. Bell states that thymic tumours occur in myasthenia gravis from a distinct group. They are all comparatively small, benign growths composed of young thymic tissue, many are hæmorrhagic. E. H. Norris is of the opinion that the pathological findings which are present in the thymus in myasthenia gravis, are best interpreted as conditions of greater or lesser degree of epithelial hyperplasia. When the hyperplasia is extreme, a localized and at times encapsulated tumour-like mass is formed. In these cases the lobular structure with its lymphocytes and Hassall's corpuscles may be obliterated and only the epithelial mass remains.

Symptomatically these tumours occur at any age. Those of carcinomatous type are most common between the ages of 20 to 40. The onset is gradual, an unproductive cough, dyspnœa, cyanosis with venous engorgement of the head and neck may be marked. Stridor and pulmonary collapse may develop. Pressure on the vagus or phrenic may stimulate or paralyze these nerves. Associated with other signs of retrosternal lesions in a high percentage of cases is the disease of myasthenia gravis and pathological changes may be found in cases of myasthenia gravis in proportion to the care with which they are sought.

This association of myasthenia gravis with tumours and hyperplasia of the thymus has long been recognized but it was not until 1936 that

Dr. Alfred Blalock removed the first tumour of the thymus in the treatment of myasthenia gravis and the first thymectomy for hyperplasia for the same disease in 1941. Both these types of cases proved satisfactory for the cure of the disease.

DIFFERENTIAL DIAGNOSIS

Myasthenia gravis is reported to be a rare disease and many practitioners pass through life without even having seen a case. This is because it is not thought of or diagnosed in the vast majority of cases. There are a number of diseases which may simulate myasthenia gravis in its variable stage of progress. Among these are the following: neurosis, psychoneurosis, ocular palsy, multiple sclerosis, the muscular dystrophies and atrophies, arteriosclerosis of the central nervous system, brain tumours, bulbar palsy, neurasthenia, hypotensive lesions, tuberculosis, post-influenzal encephalitis, narcolepsy and Plummer-Vinson syndrome. The list is rather extensive, and makes us realize where mistakes may occur in diagnosing myasthenia gravis.

SIGNS AND SYMPTOMS

Myasthenia gravis is a progressive disease of the neuromuscular mechanism, possibly upon an endocrine basis, showing periods of remission followed by an increase in the severity of its symptoms, the chief symptom being an abnormal fatiguability of the body muscles, especially and early the muscles of the eyes, 78%, and face, 61%, later involving the entire musculature. In the early stage there may be a mild intermittent fatigue relieved by a short period of rest. With the extreme muscular weakness after exertion there is a sense of hopelessness and this aggravates the already melancholy aspect so often resulting from the fallen eyelids, the hanging jaw and the snarling expression when the patient attempts to smile.

The eyes move unequally and the vision is blurred by overactivity of the eyes. Glasses are often ordered and frequently changed before the real cause for the trouble has been detected. Diplopia, dysphagia and dysarthria are very common. Speech soon becomes inarticulate. The movements of the hands and arms are awkward and weakened. It becomes difficult for the patient to even lift food to the mouth and then he or she is unable to chew or to swallow it. Because of the weakness or paralysis of the soft palate, liquids pass through the nose when swallowing is attempted. There is a weight loss with lowered resistance to infection, especially "colds", which are comomn in myasthenia gravis. The cough is feeble as the diaphragm and abdominal muscles are too weak to contract; breathing is shallow, salivation is often in excess and saliva dribbles over the lower weakened lip.

The lower limbs become easily fatigued, so much so that even a few steps are all that can be taken; it is difficult for the patient even to hold the head up or sit up. It is later noted that symptoms and signs are made worse by hot baths, infections, emotional states or gastro-intestinal upsets. Perhaps the most dangerous drug to use as in anæsthesia is intercostin (curare) for a number of cases have been lost on the table when this has been used in unsuspected cases of myasthenia gravis. Because of its direct effect upon increasing the signs and symptoms, the use of intercostin for testing the presence of the disease is to be condemned.

There are occasional complaints of sweating, "weak spells", dizziness and palpitation, not unlike attacks from hypoglycæmia, and occasionally an associated thyrotoxicosis.

Among the laboratory tests creatinine is increased; the lymphocytes may be above normal. Injection of serum from a severely ill patient has shown effects of the disease in laboratory animals. Generally speaking, there is no positive laboratory test for myasthenia gravis. X-ray findings are positive when a tumour is present. Careful technique is essential and a skilled roentgenologist should carry out this procedure as fluoroscopic positioning and stereos are most important, in outlining the presence of abnormalities of the thymus.

USE OF PROSTIGMINE

Until 1932 when Remens discovered prostigmine, the diagnosis and treatment of myasthenia gravis were difficult and discouraging. No patients were cured or satisfactorily held in check. Although prostigmine does not cure these patients, they are given a "lift" not attainable by any other drug. It was Dr. Margaret Walker in 1934 (London) who first made use of the drug in myasthenia gravis, using physostigmine (eserine). The almost im-

mediate improvement in the patient's condition with the use of prostigmine suggests that the drug acts specifically upon the neuromuscular mechanism attacked by the disease. The effect of one injection may last for eight hours.

Since prostigmine has been in use a definite method of diagnosis has been carried out and the treatment has been more encouraging. In recent years the drug has been a great help in allowing operations to be performed upon the thymic gland for myasthenia gravis. The drug has made lives happier and allowed the victims to live longer and in a higher level of activity, but to date there are no recorded cases of a cure.

No one who has seen the drug prostigmine transform, as if by magic, a listless, indifferent, melancholy vegetable into an alert attentive human with normal interests and desires will deny it a place among our indispensable therapeutic agents. Despite its transitory action with the necessity of repeated administration, it has allowed many to "take up their beds and walk".

PROSTIGMINE TEST

Added to the above benefits Veit and Schwab have shown that in prostigmine we possess a diagnostic instrument of great specificity, allowing the obscure muscular dystrophies, myopathies and other confusing neurological lesions, to be separated from myasthenia gravis. In no other disease has there been a response to the prostigmine test.

The test consists of the following procedures:

A. Determine the best objective symptoms for evidence of improvement, *e.g.*, the degree of ptosis, ability to swallow or muscle strength as measured by the ergograph.

B. Inject intramuscularly 3 c.c. (three 1 c.c. ampoules) of prostigmine, to which gr. 1/100 of atropine has been added to overcome any abdominal cramps.

C. Note time of injection.

D. At 10 minute intervals for 1 hour note in the first column the degree of improvement grading as follows: 0 no improvement; 1 slight improvement; 2 moderate improvement; 1 slight improvement; 2 moderate improvement; 3 considerable improvement; 4 complete or marked improvement.

E. In the second column, using the same grading, note the patient's subjective opinion of improvement giving value to general feeling and well-being.

F. Add up the two columns and obtain the total. The maximum score is 48. If total is less than 8 the test is negative and it is extremely unlikely that the patient has myasthenia gravis. If the score is between 8 and 18 the test is doubtful and should be repeated. If over 17 (18 to 48) the test is positive and myasthenia gravis is present.

Example:—

Time in minutes	*Objective*	*Subjective*
10	2	2
20	4	4
30	4	4
40	4	4
50	3	4
60	3	3
	20 +	21 = 41 total

SURGICAL TREATMENT

Since Blalock's historic procedures, the operations for this disease have steadily increased and now there is sufficient evidence to indicate that surgery can play an important part in the relief of the disease. A number of cures of a high percentage have been reported from various centres and in well chosen cases this percentage should increase, even as cases of toxic goitre treated by surgery showed increasing number of cures as the disease was better understood.

The publications of Mr. Geoffrey Keynes of London, Dr. Alfred Blalock of Baltimore and a number of other surgeons would indicate 70% cures or greatly improved cases following thymectomy; especially is this true in cases where tumours are present, the so-called "thymoma", and in early cases of the disease of the hyperplasia type. Suffice it to say here that myasthenia gravis is being cured in selected cases whereas without the surgical procedure there was no hope of a cure or permanent improvement.

It is now generally recognized that thymectomy is indicated in all cases where a tumour is present in the thymus or if the person with myasthenia gravis is disabled despite the fact that prostigmine medication is being employed, and that the earlier the treatment the better the results. It is possible that prolonged disease results in irreversible changes.

The technique for thymectomy is carefully planned for we are dealing with a patient whose respiratory threshold and general resistance to infection are low. With the use of prostigmine much is gained in the operative procedure and the use of penicillin injection is very beneficial. The surgical approach is through the divided sternum which is split longitudinally to the third intercostal space. By this exposure an excellent view of the entire superior mediastinum is obtained and the thymus may be seen in its entirety unlike the lateral transthoracic approach.

We wish to present two cases operated upon for myasthenia gravis, both of whom have been definitely benefited by this mode of treatment.

CASE 1

Mrs. E.G.R., aged 31. Admitted to hospital January 21, 1946. In the fall of 1941, the lady's friends noticed a dropping of her eyelids when tired and that her smile had changed to a "sarcastic" one. Later the patient noticed loss of the sense of smell and taste. These symptoms became persistently worse. She visited a number of medical men and was given variable treatment and advice. In February 1943, diplopia appeared with blurring when attempting to focus on moving objects. When she bent over there was a tendency to fall forward with difficulty in keeping her head up. When lifting average articles about the house these slipped from her fingers especially so if she was at all fatigued. Socially, she could not carry on a conversation because of inability to articulate. In 1944, the abdominal muscles and those of the legs became easily fatigued, inability to swallow normally increased, and liquids would pass out through the nose. The least exertion caused her extreme fatigue, she was rapidly becoming house-ridden and bedridden because of the above complaints. She had her tonsils removed without benefit.

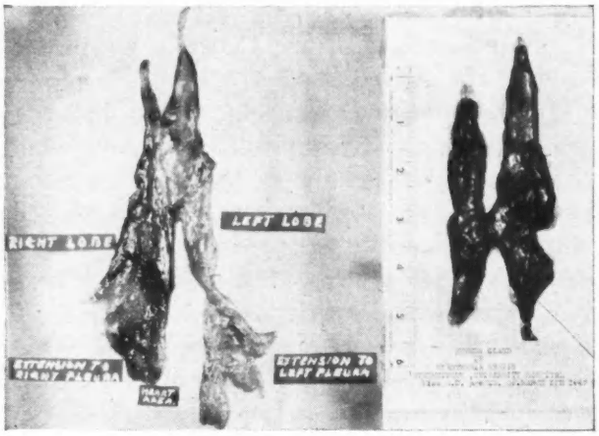


Fig. 1 Fig. 2

Fig. 1. (Case 1).—Weight of thymus 88 gm.
Fig. 2. (Case 2).—Weight 79 gm.

Upon the return of her husband from the war she came west to live in Edmonton. Upon consulting Dr. E. S. Allin of this city, the diagnosis of myasthenia gravis was confirmed. Prostigmine was given in increasing doses (5, 7, 9 tablets per day) with secondary manifestations of the drug appearing.

Under careful observation it was considered the benefit from prostigmine was not sufficient and operation was advised. The various laboratory tests and x-rays were carried out and she was put in the most satisfactory state for operation. Prostigmine and penicillin were administered pre- and post-operatively and the former was quickly reduced to 1 tablet per day following the operation.

Operation January 27, 1946.—Under intratracheal anæsthesia of nitrous oxide and oxygen and cyclopropane by Dr. Alan Hall, the sternum was split down to the 3rd intercostal space, bringing the osseous wound out to the right. The thymus was found extending from the isthmus of the thyroid to the auricles of the heart and composed of two lobes lying against the mediastinal pleura. The gland was dissected out easily and weighed 88 grams. No palpable tumours were detected. The patient made an uneventful recovery except for three days when she experienced dyspnœa and abdominal cramps, the latter most likely due to the prostigmine. These symptoms soon cleared and she was discharged from the hospital on February 14, 1946, taking one tablet of prostigmine each day. Pathological report on a small portion of the thymus shows hyperplasia as described previously.

Letters of recent date from the patient have shown steady improvement. She is able to carry on all her household duties and does not require medication. She states that she "considers herself cured of her previous disease".

CASE 2

Miss D.G., aged 22. Admitted March 4, 1947. Patient was first seen November 14, 1946, complaining of tiredness, double vision and difficulty in swallowing. For the past two years the above complaints had been present. She commenced making a "round of doctors and upon consulting one was given prostigmine, with dramatic results as she stated, but as the months passed she required larger doses of the drug and had to remain in bed most of the time since January, 1946, because of diplopia, blurring and dysphagia. At times she became melancholic, and hopelessness prevailed frequently when she attempted normal activities.

Following the clinical and laboratory examinations it was considered that surgery would be of benefit to this girl and a similar procedure was carried out with similar findings and even more encouraging results as a recent unsolicited letter indicates.

SUMMARY

The relationship of myasthenia gravis with the thymus is discussed.

The treatment of myasthenia gravis by thymectomy and a review of the surgical literature is presented.

Two operative cases are presented.

The senior author (W.C.W.) wishes to thank Dr. E. S. Allin and Dr. Frank Elliott for referring the cases and for their beneficial assistance.

BIBLIOGRAPHY

1. BLALOCK, A.: *J. Thor. Surg.*, **13**: 316, 1944.
2. *Idem*: *Ann. Surg.*, **110**: 554, 1939.
3. KEYNES, G.: *Brit. J. Surg.*, **33**: 201, 1946.
4. COHEN, H.: The British Encyclopædia of Medical Practice, Butterworth & Co., 1939.
5. SCHWAB, R. S. AND VIET, H. R.: *New England J. Med.*, **219**: 226, 1939.
6. GOOD, C. A.: *Am. J. Roentgenol. & Radium Therap.*, **57**: 305, 1947.
7. VAN DYKE, J. H.: *Anatom. Record*, **79**: 179, 1941.
8. BEST AND TAYLOR: Physiological Basis of Medical Practice, 4th Ed., 1945.

RÉSUMÉ

Deux cas de myasthénie grave avec tumeur thymique sont rapportés. Les deux cas sont des succès opératoires et cliniques. L'association myasthémie-tumeur thymique doit toujours être recherchée car dans le plus grand nombre des cas l'opération est le traitement de choix. La littérature, encore peu abondante et récente, est passée en revue. Un court rappel de la physiologie pathologique de la myasthénie met en lumière les antagonismes acétylcholine et cholinestérase et permet de déduire le rôle du thymus dans le maintien de cet équilibre pharmaco-dynamique. JEAN SAUCIER

SUBTALAR DISLOCATION OF THE FOOT*

Alexander Gibson, F.R.C.S.(Eng.) and W. B. MacKinnon, M.D., Ch.M.

Winnipeg, Man.

SUBTALAR dislocation of the foot is met with relatively infrequently in civilian practice. It is associated with fractures, major or minor, in over 80% of reported cases. Shands in 1928 reported a total of 139 cases of "subastragaloid" dislocation of the foot in medical literature up to that time. The first cases reported are credited to Judcy and Dufaurest in 1811.

Of the cases reviewed by Shands, 55.4% were of the inward type and 33.1% of the outward type; backward 3%, forward 2%. The injury was found to be six times more common in males than females. Age incidence showed the injury commonest in the third decade. Lipscomb and Ghormley, in 1943, reported 114 cases of fractures and fracture dislocations of the talus treated at the Mayo Clinic. In this group one subtalar dislocation was presented. Whalen, Boorstein and Shands have each reported a case of complete medial dislocation at the subtaloid joint without demonstrable fracture. Authentic cases of this lesion without at least minor fracture are extremely rare. Edwards and Otell reported one case of inward subtalar dislocation associated with fracture of the posterior process of the talus. The association of fracture of the posterior process and this dislocation appears to be quite frequent. Watson-Jones encountered 97 fracture dislocations of the talus and navicular during the first two years of World War II. Of this number 7 were subtalar dislocations with minor fracture. Schrock in 1942 reported 30 cases of fracture and fracture dislocation of the talus. Of this group 7 were subtalar dislocations of which 5 had minor fractures. The one case illustrated with x-rays is a medial subtalar dislocation.

The cases presented in this article are of the type of subtalar dislocation with minor fracture. The talus remains in its normal position in the ankle mortise and the remainder of the foot distal to it becomes dislocated. The only change in the position of the talus is that it usually is tilted plantar-wards in the position it would occupy in a fully plantar-flexed foot.

Normal mechanics.—The lateral movement of the foot takes place chiefly at the subtalar joint, as the heel accommodates to uneven surfaces in walking. This functional unit consists of three anatomic components: (1) The joint between the talus and the calcaneus. (2) The joint between the talus and the navicular. (3) The joint between calcaneus and cuboid. The gliding movement of the calcaneus on the fixed body of the talus is combined with rotation of the navicular on the head of the talus and this entails movement at the calcaneo-cuboid joint. The remainder of the tarsal and the metatarsal bones contribute individually gliding movements, relatively small in extent, but collectively of some importance. The movement of inversion is brought about by the action of the tibialis posterior and tibialis anterior; over-inversion is restricted by the peronei, longus and brevis. Eversion is the converse of this.

Ligaments produce static resistance to movements beyond the normal range which may result in subtalar dislocation. The chief components of this ligamentous defense are: (1) The strong interosseous talo-calcaneal ligament, occupying the sinus tarsi; it is the strongest ligament of the series which resists inversion and eversion. (2) The calcaneo-fibular ligament which especially resists inversion. (3) The posterior talo-calcaneal ligament is a relatively weak ligament which aids in resisting forward or backward movements of the calcaneus on the talus. (4) The portion of the deltoid ligament attached to the sustentaculum tali and the navicular and the margins of the calcaneo-navicular ligament.

Blood supply of the talus.—Lipscomb and Ghormley state that the greater part of the blood supply of the talus is derived from a branch of the dorsalis pedis artery which enters the lateral aspect of the neck of the talus. The smaller part is supplied from ligamentous and capsular attachments. McKeevor maintains that the entire blood supply of the talus is derived from a branch of the anterior tibial artery. He found evidence also that the artery which eventually breaks up into several nutrient arteries, is carried in the superior talo-navicular ligament. Gibson and Inkster in 1934 in an article on fractures of the talus stressed the importance of blood supply through ligamentous attachments, especially the deep surface of the deltoid ligament. It was found that in cases where the body of the talus was grossly displaced and projected through the interval between the flexor hallucis longus and the flexor digitorum longus, aseptic necrosis was likely to occur.

It is interesting to record that in the cases of subtalar dislocation without major fracture herewith described aseptic necrosis has not been observed. In the

* From the Department of Orthopædic Surgery, Deer Lodge Hospital, Department of Veterans' Affairs, Winnipeg.

medical literature on the subject no case has been encountered in which this complication occurred.

Nomenclature.—The terms used in describing dislocations of the foot are not standardized. Taking the head of the talus as a fixed position, the terms medial, lateral, upwards, downwards and rotatory can be used to describe subtalar dislocations. In the medical literature on the subject, inversion or adduction are alternative terms for medial dislocation, and eversion or abduction as alternative terms for lateral.

Mechanism.—It is probable that this lesion occurs with forced plantar flexion of the foot. Evidence in favour of this is the history of injury which is usually falling or stepping from a height and landing forcibly on the forepart of the foot. Examples of preceding trauma are falling with the foot caught in the rung of a ladder or the foot rail of an automobile. Upward, downward, medial, lateral or rotatory dislocation occurs due to excessive force applied in a corresponding line. It is notable that this suggested mechanism is in contrast to that of major fractures and fracture dislocations of the talus. Many of these occur by forced dorsiflexion of the foot.

The minor fractures occurring are believed to be due to the pull on ligamentous attachments,

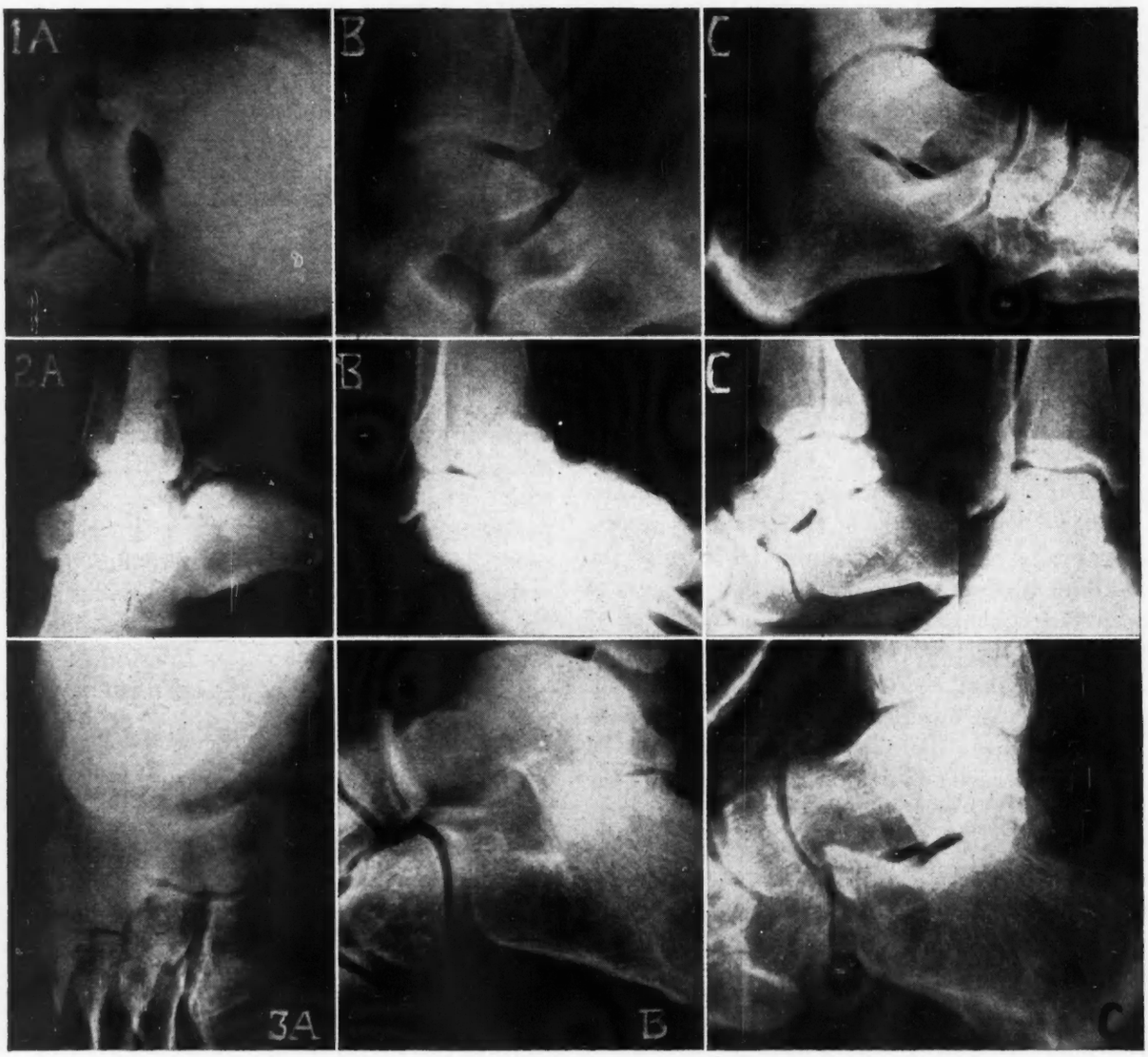


Fig. 1.—(A) Dorsal plantar view on admission September 30, 1945. (B) Oblique view on admission September 30, 1945. (C) April 1, 1946, 6 months after reduction. **Fig. 2.**—(A) November 6, 1946, lateral view on admission. (B) November 6, 1946, antero-posterior view on admission. (C) November 26, 1945, antero-posterior and lateral views following reduction. **Fig. 3.**—(A) November 21, 1945, on admission to Winnipeg General Hospital, dorsal plantar view. (B) November 21, 1945, lateral view on admission. (C) November 22, 1945, following reduction.

and the usual one is a fracture of the posterior process of the talus from the pull of the posterior talocalcanean ligament. That is, they are traction or sprain fractures.

Reduction.—Reduction of these dislocations has been accomplished by a relatively uniform, closed procedure. The knee joint is flexed to a right angle to relax the tendo achillis. The distal segment of the foot is strongly plantar flexed in order to disengage the dislocated bones. At the same time strong traction is maintained with movements to replace the bones in normal relationship. The manœuvre is usually accomplished without difficulty. Open reduction may be required for cases seen as late as two weeks following injury.

RESULTS

All authors consulted emphasize the relative ease of closed reduction in cases treated early. The function of the foot following closed reduction has been good. No case of aseptic necrosis of the talus has been encountered in the available literature, nor have secondary operative procedures been required for traumatic arthritis of the subtalar joint.

CASE 1

H.C., aged 72 years. Pensioner. On September 30, 1945, he was walking across a wooden culvert which gave away. He jumped sideways and landed on something solid at the bottom of the ditch. On examination malleoli appeared intact. Deformity began distal to the malleolus. The rest of the foot including the calcaneus appeared dislocated laterally on the talus. X-ray revealed subtalar dislocation of the foot of the lateral type. Some irregular fragments laterally appear to come from the lateral malleolus (Figs. 1A and 1B). Reduction under pentothal anæsthesia. By angulation and traction, position of the calcaneus in relation to the talus was restored. Manœuvre was repeated and the navicular reduced into normal contact with the talus. Plaster was applied from the knee to the metatarsal heads. Foot elevated on a Braun splint.

October 16.—Plaster changed, left foot ankle in normal position.

November 16.—Plaster removed. Ankle and foot exercises begun.

November 29.—Can walk without ankle support and without pain. Ankle motion still restricted.

April 1, 1946.—Walks with a cane. Slight limp. A few degrees limitation of inversion and eversion. Full range of ankle motion. Lift of ¼" placed on inner side of sole and heel of shoe (Fig. 1C).

October 15.—Walks with a cane. X-ray shows some persisting osteoporosis. Movements of subtalar joint restricted about 25%.

CASE 2

M.C.K., aged 24 years. On November 6, 1945, was knocked down by a street car, sustaining injury to right foot, laceration of the left knee, bruising of the back and lacerations of left forehead. The laceration at the back of the left knee was sutured.

Diagnosis.—(1) Medial subtalar dislocation of foot with fracture of the posterior portion of body of talus (Figs. 2A and 2B). (2) Compression of second lumbar and slight collapse of anterior superior angle of fourth and fifth lumbar vertebræ. Reduction of foot dislocation was accomplished by manipulation under anæsthesia (Fig. 2C). Plaster from tibial tubercle to toes.

February 19, 1946.—Posterior fragment of talus appeared to be united. Plaster removed.

March 28.—Left ankle movements are painless and he is able to walk a mile without any discomfort. Dorsiflexes to 68°. Plantar flexion to 103°. Inversion and eversion limited.

October 15.—Full range of inversion and eversion and of plantar and dorsiflexion. No complaints.

CASE 3

J.D., aged 56 years. November 14, 1945, injured left ankle in stepping off of a train. Plaster was applied. Admitted to hospital 7 days following injury.

November 21.—Diagnosis of internal rotation dislocation of talo-navicular joint was made. Fracture posterior part of body of talus (Figs. 3A and 3B). Closed reduction. Plaster.

November 22.—X-ray films satisfactory following reduction (Fig. 3C).

January 7, 1946.—Plaster removed. Crepe bandage applied.

February 5.—At full work as a commercial traveller. Carries a small sample bag.

February 11, 1947.—Reports by letter is not hindered at all in work and able to walk without a limp and to run.

CASE 4

Mrs. R., aged 29 years. July 31, 1946, while getting out of automobile went over on left ankle. Admitted to hospital same day. X-ray showed medial subtalar dislocation of the foot with fracture of posterior process of talus. Reduction and plaster from below knee to toes under general anæsthesia. Plaster left on for 6 weeks. Full functional recovery.

SUMMARY

1. Four cases of subtalar dislocation of the foot with minor fractures are described.

2. Two patients are without symptoms more than a year after injury. One is asymptomatic after six months. One, aged 72 years has minimal disability.

3. The mechanism of this injury and method of reduction are described.

The authors wish to express their appreciation to Dr. Elmer S. James, F.R.C.S., for supplying details of Case 4.

BIBLIOGRAPHY

1. BOORSTEIN, S. W.: *J. Bone & Joint Surg.*, 15: 1026, 1933.
2. DUFAUREST, P.: *J. de Corvisant*, 22: 348, 1811.
3. EDWARD, J. F. AND OTELL, L. S.: *Radiology*, 14: 71, 1930.
4. GIBSON, A. AND INKSTER, R. G.: *Canad. M. A. J.*, 31: 357, 1934.
5. JUDCY, P.: *Bull. Fac. Med.*, 11: 81, 1811.
6. LIPSCOMB, P. R. AND GHORMLEY, R. K.: *Surg. Clin. N. Am.*, 23: 995, 1943.
7. MCKFEVOR, F. M.: Fracture of the neck of the astragalus (unpublished thesis), 1939; quoted by Schrock, *et al.*, *J. Bone & Joint Surg.*, 24: 560, 1942.
8. SCHROCK, R. D., JOHNSON, H. F. AND WATERS, C. H. JR.: *J. Bone & Joint Surg.*, 24: 560, 1942.
9. SHANDS, A. R.: *J. Bone & Joint Surg.*, 10: 306, 1928.
10. WALEN, I.: *J. Bone & Joint Surg.*, 25: 211, 1943.
11. WATSON-JONES, R.: Injuries to Bones and Joints, Vol. 2, 2nd ed., 1942.

INSULIN RESISTANCE IN DIABETES COMPLICATED BY HYPERTHYROIDISM*

Walter de M. Scriver, M.D., F.R.C.P.[C.]

Montreal, Que.

IN his biography of Sir Frederick Banting, Lloyd Stevenson[1] discusses the fate of the diabetic who, prior to the advent of insulin, slipped into the ketosis and coma that ended in death, contrasting the picture with that of the present day diabetic in these words: "All this in the absence of insulin, all this . . . transposed into the past tense. All this while the helpless physician stands, or rather stood, with his hands tied and his mind and heart clouded with frustration and despair. All this in the years before Banting."

Such is the picture recalled to the mind of those of us who remember the tragic hours spent with those diabetic patients before the days of insulin. Many today have never experienced that feeling of utter helplessness that arose when the diabetic patient began to slip into coma, because, with our present day handling of the problem with insulin, failures are few and then usually because the patient has been too long in coma before insulin has been used. However, since we still have those rare cases which do not respond to modern treatment, and it has been my fate in the past year to stand with my "hands tied and mind and heart clouded with frustration and despair", I wish to report a case of diabetes which proved to be so resistant to insulin that she followed the course of the diabetic of the pre-insulin era and slipped into a ketosis that we failed to stop.

On March 20, 1947, a 41-year old married woman was admitted to the Homœopathic Hospital suffering from hyperthyroidism and diabetes. According to her history, she had had a swelling of her neck ever since she was a young girl, but it had given her no trouble until 1940, when it began to increase in size. In the spring of 1941 she noticed that she was losing weight, and finally in November of that year she consulted her family physician who had her admitted to hospital for a five day period, during which time he found that she had a glycosuria and a fasting blood sugar of 246 mgm. %. There is no record of the size of the thyroid at that time, nor of a basal metabolic rate determination. The pulse rate, however, varied from 72 in the morning to 100 later in the day. She was placed upon a dietary regimen low in fat, moderately high in carbohydrate and protein, and was given 30 units of protamine zinc insulin daily before breakfast. Two days later, although glycosuria persisted in the 24-hour urine, the fasting blood sugar was reported as 98 mgm. %, and she was discharged with directions to follow this regimen.

The history for the next few years is rather sketchy, but apparently she followed her instructions in a rather desultory fashion, with poor control of the diabetes, until early in 1946 when she discontinued her insulin because she did not feel any better.

About this time her family physician died and she sought no medical advice until early in March of 1947 when she consulted another physician because she was not feeling well and had lost weight from 145 to 125 lb. She admitted that for some time she had suffered from nervousness and palpitation of the heart, and that she perspired excessively and preferred to be in a cold room rather than where it was warm. When she was examined, her physician found that the thyroid was diffusely enlarged; there was a fine tremor of the outstretched hands, the pulse rate was 120; the blood pressure was 170/110, but there were no abnormal eye signs. Glycosuria was present and blood sugars on March 8 were at the high levels of 277 mgm. % in the fasting state, and 333 mgm. % one and one-half hours after her breakfast. A few days later the basal metabolic rate was found to be plus 33 in a satisfactory test. She was advised to follow her old dietary regimen, and to take 40 units of protamine zinc insulin daily while awaiting admission to hospital.

Soon after her admission to hospital I was asked to see her in consultation, and found the condition as outlined above: we were apparently dealing with hyperthyroidism in a diabetic who had paid little attention to a proper regimen. She was placed on her original diet of 70 gm. of protein, 50 gm. of fat, and 250 gm. of carbohydrate, and given 50 units of protamine zinc insulin daily before breakfast. At the same time Lugol's solution was commenced in the dosage of ten drops three times

* Presented at the annual meeting of the Royal College of Physicians and Surgeons of Canada, November 28, 1947.

daily. For the first two days there was considerable glucose, and a trace of ketone bodies in the 24-hour urine, and the fasting blood sugar was 210 mgm. %. She appeared to be in good general condition and took her full diet. The insulin was changed to crystalline in divided doses and later to protamine zinc and divided doses of crystalline up to a total of 112 units daily, under which regimen the ketone bodies disappeared from the urine, and glycosuria lessened but did not disappear. The blood sugars, however, still remained high with levels of 244 mgm. % fasting, and 282 mgm. % before the noon meal, four hours after the morning insulin. Thus in spite of increasing doses of insulin there was no demonstrable effect upon the blood sugar level, though the ketonuria had cleared. As there was no evidence of an infectious process, or other apparent cause for the lack of response to insulin, it was thought that it might well be due to the hyperthyroid state; if such were the case it was reasonable to hope for an improvement in the diabetic condition if a remission of the thyrotoxic state could be induced by treatment with Lugol's solution. Such expectations, however, were not realized, and although by March 29 the patient was free from toxic symptoms and signs and the basal metabolic rate had fallen to plus 8, yet there was still a mild but decreasing glycosuria, with no ketonuria, on a daily dosage of 144 units of insulin including both crystalline and protamine zinc.

We were now on the horns of a dilemma; if thyroidectomy were not carried out within the next few days the patient would pass through the stage of iodine-remission and re-develop toxic symptoms with a bad influence upon her diabetic state; if the operation were done, it would be upon a poorly controlled diabetic, with all the risks associated with the state of uncontrolled hyperglycæmia. Accordingly, a frank discussion was held between patient, physician, and surgeon during which it was decided that the course that seemed the lesser of the two evils was to operate and so remove the thyroid factor, particularly as there was no longer any sign of ketosis, in the presence of which operation would have been definitely contraindicated.

Accordingly, on March 31, subtotal thyroidectomy was carried out without untoward incident, under pentothal anæsthesia with the addition of a small amount of cyclopropane and ethylene by endotracheal tube. The total time of operation from the commencement of anæsthesia to completion of the operation was exactly one hour, and the condition of the patient remained good throughout. Before she went to the operating room she was given 10 units of crystalline insulin, and on return she received two intravenous injections containing 50 gm. of glucose each, and 20 units of crystalline insulin subcutaneously with each.

The immediate postoperative course was uneventful, there was no nausea or vomiting, and although she felt somewhat nervous, the patient slept well that night. The 24-hour urine for the day contained a moderate amount of glucose, but no ketone bodies.

On the following day she appeared to be well, and was given liquid feedings containing 20 gm. of carbohydrate at three-hour intervals, which were well tolerated. Twenty units of crystalline insulin were given with alternate feedings for a total of 60 units in the day. The urine for this day contained more glucose and a trace of ketone bodies was present. The blood sugar 3 hours after the morning dose of insulin was still high at 235 mgm. %.

In spite of this, the patient felt so well on the third day that she told her husband that she was ready to return home. She was able to take and enjoy her full preoperative diet, and was given 32 units of crystalline insulin with each meal for a total of 96 units. However, the urine still contained glucose and a trace of ketone bodies. On the fourth day she appeared to be quite well until the early afternoon, when she complained of nausea and soon vomited about 50 c.c. of fluid. Because of these symptoms, and the finding of a blood sugar level of 339 mgm. %, at 5.30 p.m. 100 units of crystalline insulin was given intravenously along with 1,000 c.c. of 5% glucose saline. Five hours later the blood sugar had reached 430 mgm. % and there was still a moderate reaction for ketone bodies in the urine. Accordingly, 20 units of crystalline insulin were given at once, and repeated for three more doses during the night, making a total of 276 units during the 24-hours.

In spite of these doses of insulin, by the morning of the fifth day the clinical picture of the patient was that of classical diabetic ketosis, with moderate Kussmaul breathing, ketone odour to the breath, soft eyeballs, dehydration,

and vomiting, but she was still fully conscious and mentally active. Forty units of crystalline insulin had been given at 9.00 a.m., but with the change in the clinical state, and the finding of continued glycosuria and ketonuria and a blood sugar level of 420 mgm. %, 100 units of crystalline insulin were given intravenously every hour from 11.00 a.m. In the faint hope that we might have been dealing with an inert preparation of insulin, a new lot with a different serial number was procured, and used. Sodium lactate was also given intravenously in M/6 solution, but her condition continued to deteriorate.

On the suggestion of Dr. E. H. Mason that there might be an element of thyroid toxicosis, we gave 5 c.c. of Lugol's solution intravenously with normal saline while continuing the large doses of insulin. None of these measures, however, appeared to have the slightest effect, and the patient progressed rapidly into the comatose state, dying at 9.00 p.m., about 28 hours after her first vomiting attack. During this time she had received 1,000 units of insulin, 50 grams of glucose intravenously, as well as 5 c.c. of Lugol's solution and 960 c.c. of M/6 sodium lactate solution. The last blood sugar determination on a sample taken at 4.00 p.m. was 434 mgm. %.

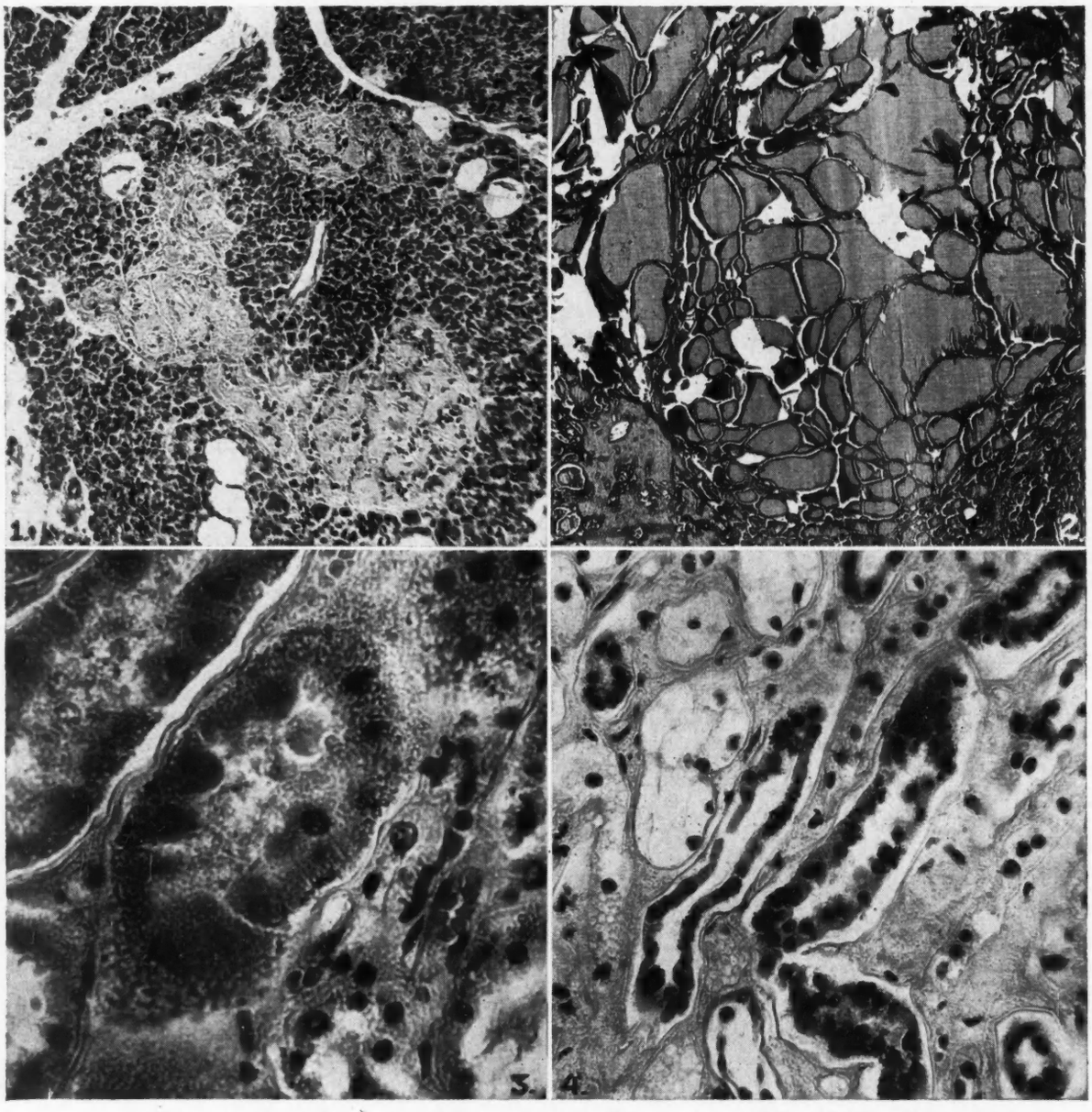


Fig. 1.—Section of pancreas showing hyalinization of the islands of Langerhans and deposit of pigment in a small duct (upper left centre). **Fig. 2.**—Thyroid showing small hyperplastic acini and large acini filled with colloid. **Fig. 3.**—Kidney—convoluted tubules. The pigment is deposited as fine dots at the base of the cells. **Fig. 4.**—Kidney—collecting tubules. The pigment is coarser, and frequently fills the whole cell.

At autopsy, which was carried out approximately twelve hours after death, the recent thyroidectomy wound was found to be clean and well healed; a small amount of thyroid tissue was present, and was taken for section. While the thoracic organs were grossly normal, in the abdomen posterior to the foramen of Winslow and about the cœliac axis the tissue was swollen, boggy and œdematous and in it enlarged soft lymph nodes could be identified. The spleen was soft in consistency and weighed 250 gm.; the liver was normal but a small calculus 2 mm. in diameter was found in the common bile duct, which was patent. The pancreas was smaller than normal, weighing 50 gm. Both kidneys were somewhat enlarged and flabby and weighed 175 gm. each. There was no gross lesion evident in the brain.

In the histological studies of the pancreas there was found hyalinization of many of the islands of Langerhans, with many normal islands as well. Hyaline changes were present in the vascular channels, and the smaller ducts often contained bile-like greenish-yellow pigment, either filling the lumen, or deposited upon the surface or within the walls; this pigment was iron-negative. In the liver there was an unusual amount of intranuclear glycogen in the parenchymal cells, particularly about Glisson's capsule. The bile ducts were normal.

The tissue from about the cœliac axis consisted of extremely œdematous lymph nodes with œdema of the surrounding tissues, this œdema had led to marked separation of the lymphoid and reticular elements, with loss of germinal centres and topographical markings. There were no areas of necrosis, though many cells displayed imbibition and dissolution. Some lymphocytes were plasmocytic, and Russel bodies were present. Pigmentation was not a feature. Both kidneys presented the same histological picture; besides a moderate degree of hyaline change in the arterioles and parenchymatous degeneration of the epithelium, there was a marked deposition of a dark yellowish pigment which was negative to iron stains and was suggestive of bile. It was present to a greater extent in the convoluted tubules of the cortex, and the collecting tubules of the medulla. In the former it was deposited as very fine dots at the base of the cells; in the collecting tubules it was coarser, often filling the whole cytoplasm. The glomeruli were hyperæmic but essentially free from pigment. The adrenals and pituitary appeared to be normal; the thyroid tissue was made up of areas of small hyperplastic acini separated by fibrous septa from areas of large colloid filled acini, the picture being essentially the same as that seen in sections of the tissue that was removed at operation.

DISCUSSION

There are now numerous reports in the literature of patients who have been resistant to insulin; in general they can be classified in groups according to associated conditions which include: (1) infections; (2) severe acidosis of diabetic coma; (3) diseases of the other endocrine glands; (4) disease of the liver; (5) allergy (with allergic resistance to insulin); (6) no obvious cause.

In our case we could find no clinical evidence of infection, and at autopsy the only significant finding was the adenopathy of a localized nature with no evidence of primary focus. While this patient died in acidosis and coma yet she was resistant to insulin before her operation and was receiving a fair dose of insulin before she went into ketosis. Although the thyroid gland was abnormal, no evidence of disease could be made out in the pituitary or adrenals, and her thyroid condition appeared to be under control even when the diabetes was not. There was no evidence of liver disease either clinically or at autopsy, nor were there ever any signs or symptoms of an allergic state.

It has long been recognized clinically that hyperthyroidism has an unfavourable action upon diabetes, but there are not many reports in the literature of such cases. In a relatively large series of cases who had both diabetes mellitus and hyperthyroidism, Joslin and Lahey[2] found that the use of insulin, diet, and iodine gave good results in preparing these patients for operation and in carrying them through convalescence. No serious attempt was made before operation to make the urine completely sugar-free with insulin and diet, and it was noted that after operation there was a sudden temporary increase in glycosuria, which had no ill effects upon the general course of convalescence. Three cases died after operation, one in thyroid storm, one after the difficult removal of an intrathoracic goitre; the details of the third are not given.

Root[3] has described two patients with diabetes and hyperthyroidism, both of whom went into ketosis: the first improved with insulin, but ultimately relapsed and died in ketosis induced by a streptococcus infection; whereas the second was easily brought out of ketosis and later underwent a successful thyroidectomy without further complications. In discussing these cases Root states, "The rapidity of the onset of coma was almost matched by the rapidity of recovery under treatment". Neither of these cases required excessively large doses of insulin to control the ketosis and the diabetic state.

A case very similar to ours has been reported by Hills,[4] a diabetic with hyperthyroidism who maintained persistently high blood sugar levels in spite of relatively large doses of insulin, and went into ketosis on the tenth day after thyroidectomy. She was brought out of this ketosis with 220 units of insulin and intravenous administration of sodium bicarbonate, but later developed pneumonia and after a stormy course was again brought out of ketosis but left with a residual hemiplegia. He states, "During the postoperative period there was a marked inability to metabolize glucose, and this could not

be controlled even by the administration of massive doses of insulin."

In discussing a larger series of cases of diabetes complicated by hyperthyroidism, Wilder[5] states that these patients always require more insulin than is needed in an uncomplicated case, and that after thyroidectomy it is necessary to watch closely to avoid ketosis on the one hand, and hypoglycæmia on the other. So susceptible does he find them to hypoglycæmia that he suggests that it is well not to attempt too rigid control of the diabetic condition. In her studies on the effect of insulin in rabbits Zeckwer[6] found that some apparently normal animals which were "naturally" resistant to insulin, became less so after thyroidectomy, although a considerable degree of resistance still remained in those rabbits who before operation had been very resistant. No satisfactory explanation could be found for this condition.

A case of resistance to large doses of insulin in a patient who ultimately died in coma has been reported by Root.[7] At autopsy the findings were those of hæmochromatosis, which had not been suspected clinically. While our case had the resistance to insulin and pigment was found in several organs, yet the diagnosis of hæmochromatosis cannot be made as the pigment gave a negative reaction for iron. Mason[8] has reported a case of diabetes in which at times the blood sugar levels were unaffected by large doses of insulin, at other times there were relapses into severe hypoglycæmic levels without warning. The patient ultimately died in diabetic acidosis in spite of insulin therapy, and was found at autopsy to have a cyst of the roof of the 4th ventricle. We have found no evidence of lesion in the brain of our patient. A somewhat similar clinical case was reported by McGavack *et al.*,[9] who required large doses of insulin and at times went into hypoglycæmia; prolonged periods of ketosis occurred without clinical evidence of coma. In reviewing the other remaining cases reported they state, "The majority of these insulin resistant patients stand ketosis well", which was not the case in our patient.

Although Lozinski and Froelich's[10] case had no evidence of thyroid disease, yet she was largely resistant to insulin and took as high as 3,600 units daily, on which regimen she would have severe hypoglycæmic reactions at times. With threatening acidosis they gave doses as high as 1,000 units and succeeded in clearing the ketosis. After irradiation of the pituitary gland the patient improved greatly and was reported, 16 months later, as controlled with 40 units daily. In the most recent report on insulin resistance Axelrod[11] and others concluded that the improvements in tolerance that occurred in their own cases were spontaneous, and not related to any of the therapeutic measures employed, and that with our present state of knowledge we have still a group of cases in which we are unable to explain satisfactorily the reason for, or mechanism of, insulin resistance.

In our own case, while the cause of the failure of insulin is not clear, yet it is evident in retrospect that several other different courses might have been followed. Had operation been postponed, the hyperthyroid state would have returned, with the associated poor effect on the diabetic process and the general metabolism. As she had already received iodine, the effect of thiouracil or its related compounds would have been considerably delayed, but ultimately the thyroid toxicity would have come under control, though there would still remain the dangers due to the drug itself. Finally, much larger doses of insulin could have been used, in the hope that even greater doses might have had some effect on the blood sugar which we had not been able to attain previously.

We can only surmise what might have been the result had any of these alternative courses been followed; certainly they would not have been without danger, but the ultimate result might well have been better.

Grateful acknowledgment is made, for clinical history details, to Dr. Lyla Brown and Dr. J. J. Griffith, and for the complete autopsy report to Dr. T. R. Waugh.

REFERENCES

1. STEVENSON, L.: Sir Frederick Banting, Ryerson Press, Toronto, p. 113, 1946.
2. JOSLIN, E. P. AND LAHEY, F. H.: *Am. J. M. Sc.*, **176**: 1, 1928.
3. ROOT, H. F.: Medical Papers Dedicated to Henry A. Christian, Waverley Press, Baltimore, 1937; also in *Tr. Am. Clin. & Climatol. A.*, **51**: 1, 1935.
4. HILLS, R. G., SHARPE, J. C. AND GAY, L. N.: *Bull. Johns Hopkins Hosp.*, **55**: 193, 1934.
5. WILDER, R. M.: *Arch. Int. Med.*, **38**: 736, 1926.
6. ZECKWER, I. T.: *Am. J. Physiol.*, **106**: 273, 1933.
7. ROOT, H. F.: *New England J. Med.*, **201**: 201, 1929.
8. MASON, E. H.: *J. Clin. Invest.*, **9**: 31, 1930.
9. MCGAVACK, T. H., KLOTZ, S. D., VOGEL, M. AND HART, J. F.: *J. Clin. Endocrinol.*, **6**: 747, 1946.
10. LOZINSKI, E. AND FROHLICH, L. I.: *Canad. M. A. J.*, **46**: 62, 1942.
11. AXELROD, A. R., LOBE, S., ORTEN, J. AND MYERS, G. B.: *Ann. Int. Med.*, **27**: 555, 1947.

CASE REPORTS

METHÆMOGLOBINÆMIA IN AN INFANT

Nathan Goluboff, M.D.

Saskatoon, Sask.

Recently there have been reported, in rural areas, in infants under two months of age, a few cases of cyanosis, caused by methæmoglobinæmia, due to ingestion of contaminated well water with a high nitrate content. It is felt that since this is but a newly recognized clinical entity, and since only a very few cases have been reported, it is worthwhile adding another similar case, the first to be reported from Saskatchewan.

Baby T.C. was a two month infant, born May 16, 1947, and first seen by me on July 10, 1947. The baby was born in a small country hospital. He was a first child, born of a healthy young mother. Labour was uneventful, as was the course in hospital. Patient and mother were discharged after ten days.

The baby was breast-fed for the first week, following which an evaporated milk formula was given. Within a few days after discharge from hospital the infant developed a peculiar bluish cyanosis which became quite marked at irregular intervals. At one month of age the cyanosis became obviously severe. The local physician who examined the infant could not account for the cyanosis, the temperature being normal and physical examination being otherwise completely negative, except for a laboured respiration, and general appearance of anoxia. It was felt that there must be some fulminating overwhelming infection present and the child was admitted to hospital. X-ray of chest was negative.

Penicillin was given intramuscularly, and oxygen was administered. The child's colour and general condition improved within a few days, the temperature remaining normal. However, a few days after discharge from hospital, the spells of cyanosis recurred, and to a milder degree cyanosis was constantly present. The child, however, did not again appear otherwise ill. Crying had no apparent effect, nor was cyanosis related to feeding. There were no signs of respiratory obstruction. There was no diarrhœa.

I first saw the child on July 10. The infant had been in the city overnight, and the mother said it looked better than usual. The colour was definitely abnormal, a pasty greyish hue, with blue tinge, especially around the eyes and lips. The infant weighed eleven pounds, was well nourished and development was normal for age. Respiration was normal, and crying did not affect the colour. No other abnormalities could be found on careful examination. The heart appeared perfectly normal and no murmurs were heard.

I recalled recent articles on methæmoglobinæmia in infants caused by contaminated well water. The local hospitals were unable to do a methæmoglobin estimation which was only available at the University Biochemistry Department. Due to the late hour the mother was told to bring the child to the City Hospital out-patient department for x-ray examination and a blood specimen the next morning.

On the next morning the child presented a completely different picture, and had a normal rosy complexion. The mother stated it had never looked like this, since the first two weeks of life. A methæmoglobin estimation was therefore unfortunately not obtained. The blood count was normal, except for a mild anæmia, hæmoglobin 64% (9.9 gm./100 c.c.). X-ray of heart and lungs was normal. The infant remained in the city for a week but no recurrence of cyanosis took place, at any time.

Analysis of the well water used was obtained shortly, and was found to contain nitrite 0.04 parts per million, and nitrate 212.7 parts per million. The well was called the Livery Barn Well, and opportunities for contamination were obvious. The three other local wells on which reports were obtained had nitrate contents of 13.3, 26.6, and 106.4 parts per million. Ten parts per million of nitrate is considered the upper limit for a safe supply. The mother tried the same well for a few days, and again noted a slight bluish coloration of the skin. The water supply was then obtained from another well, following which no cyanosis has recurred.

There is no intention of reviewing the subject, which was recently done in this *Journal* by Medovy *et al.* However it may be well to briefly re-iterate the factors involved. Water, contaminated by animal and vegetable water seepage, may have a high nitrate content of several hundred or more parts per million. The nitrate is converted to nitrite in the bowel, and excreted as ammonia. Normally the nitrite is not absorbed, but in these tiny infants, all of whom have been under two months of age, nitrite may be absorbed, and acts directly on the hæmoglobin to form methæmoglobin, which may cause a bluish cyanosis when it exceeds 3 gm. %, and may cause signs of anoxia, when it forms a large enough percentage of the hæmoglobin, and reduces the oxygen-carrying proportion sufficiently.

A few points of practical interest may be worth noting. The high nitrate content of water, in poorly constructed or poorly placed wells, is caused by animal excreta and organic waste and surface water drainage. Some such wells may be satisfactory bacteriologically for drinking purposes, but still have a high nitrate content, because when filtering through soil the larger organic particles and bacteria are filtered out, but the soluble nitrates remain. How commonly high nitrate content occurs in well water, has not been ascertained, as in routine examination of water supplies nitrate content determination is not done in Saskatchewan, nor apparently elsewhere.

Why more cases are not recognized is not clear. On questioning a number of physicians with years of experience in rural practice, none could recollect similar cases of cyanosis, of unknown origin. In this case a neighbour's infant of identical age and on similar formula, using the same well water showed no apparent abnormal colour of the skin. It has been recommended by some authorities that dry milk or evaporated

milk formulæ be avoided in rural areas, because of the large amount of water used, with opportunity for the above condition to develop. However, in view of the relative rarity of its reported appearance, it does not seem wise at this time to give up the use of evaporated milk, which is probably the safest milk supply in most rural areas.

However, it may be advisable that routine examination of water supplies should include a nitrate estimation. Where the nitrate content is known to be excessive, evaporated or dry milk formulæ should be avoided, and safe whole milk formulæ used, with the much lesser amount of water required. Of course, the preferable procedure, where at all possible, would be to use another satisfactory well, and meanwhile measures taken to correct the poorly constructed or poorly located well.

Since most cases will be noted in rural areas, it seems important for the practitioner to know how to make a definite diagnosis. Since methæmoglobin is re-oxidized to oxyhæmoglobin upon standing in contact with oxygen, it is necessary to make the estimation as quickly as possible after blood is withdrawn. For this reason it may not be profitable to depend on a sample of blood sent from a country point to a proper laboratory for methæmoglobin estimation. Locally, at the University Biochemistry Department, human blood laked with water 1:5 dilution and containing initially 8 to 29% of hæmoglobin as methæmoglobin decreased to about one-half in 24 hours, at room temperature. An abnormal level would probably still be detectable. However in an infant, where there is cyanosis caused by this condition, the blood grossly has a typical chocolate appearance, as is seen in other types of methæmoglobinæmia, and can be seen when the blood is drawn in the syringe.

For the actual spectroscopic estimation 1 c.c. of oxalated or citrated blood (preferably sterile) would be sufficient, and the test tubes immediately corked. The blood nitrite in a few cases has been estimated and reported as high as 100 gammas per 100 c.c. The normal is 10 (range 0.5 to 29) and at least 10 c.c. of blood would be needed for this estimation. Of course, the obvious procedure, in any case suspected, is to change to another water supply, and have it and the water previously in use, checked for nitrate content immediately. The cyanosis will improve as the methæmoglobin is converted to oxyhæmoglobin, and usually, as in this case, almost completely within 36 to 48 hours.

In the treatment, methylene blue intravenously has been used and recommended in severe anoxic cases, where immediate measures seem necessary, and effects a remarkable and instantaneous cure. The difficulty, I believe would be in most rural points to have this method available. The methylene blue is put up in ampoules of 10 to 100 c.c. of 1%. However, on inquiry locally no methylene blue ampoules were available at a 300 bed hospital, nor at any large local drug houses. I was informed its manufacture had been discontinued by Parke Davis & Co., but was obtainable from William H. Rorer Inc. of Philadelphia, and that British Drug Houses listed a 1 c.c. ampoule of 5% methylene blue which can be diluted to 1% for intravenous use. Therefore in most rural points, it certainly would not be obtainable when needed.

Methylene blue, if of a high chemical purity, can be prepared locally by making a 1% solution and sterilizing by autoclave. This can be administered in doses of 1 to 2 mgm. per kilogram of body weight intravenously, but should not be recommended except in urgent cases. In cases which are less severe the methylene blue can be successfully administered in dosage of 10 to 20 mgm. of the dye, for each kilogram of body weight (dissolved in water or 5% dextrose solution), although this is occasionally accompanied by vomiting and diarrhœa (65 to 100 mgm. per kilogram orally is advised by others). There is no difference between methylene blue used commonly for staining purposes and that used for oral use or intravenous solution, providing it is of a high pharmaceutical grade. The dose can be repeated several times, at four hour intervals, depending on the clinical response.

SUMMARY

A case is described of undoubted methæmoglobinæmia in a two-month infant, caused by ingestion of contaminated well water with a high nitrate content, and diagnosed clinically. Some practical points which may arise in diagnosis and treatment are discussed.

Physicians must be on the alert for this condition, in which the cyanosis may be so easily attributed to congenital cardiac or respiratory abnormalities, or to coincidental infections. Lack of recognition of the underlying cause, may in

some cases lead to dangerous and even fatal results.

BIBLIOGRAPHY
1. MEDOVY, H. *et al.*: *Canad. M. A. J.*, **54**: 505, 1947.
2. FERRANT, M.: *J. Pædiat.*, **29**: 585, 1946.
3. FAUCETT, R. L. AND MILLER, H. C.: *J. Pædiat.*, **29**: 593, 1946.
4. WALLACE, M. W.: *J. Am. M. Ass.*, **133**: 1280, 1947.

MALIGNANCY DEVELOPING IN FAMILIAL POLYPOSIS OF COLON IN MALE TWINS

J. P. Wyatt, M.D. and H. Goldenberg, M.D.

Toronto East General Hospital, Toronto, Ont.

The simultaneous occurrence of tumours in twins, whether monovular or binovular, is of great interest. The development of carcinoma of the large bowel in twins with familial polyposis of the colon is of even greater interest.

CASE 1

M.R., aged 23, was first admitted in July, 1942, to a military hospital complaining, since 1940, of bleeding from the rectum on defæcation. Physical examination was negative, but sigmoidoscopic examination revealed multiple polypi of the rectum and colon. A biopsy from a polyp in the rectosigmoid region was taken, which on microscopic examination was diagnosed as adenocarcinoma by a competent authority. The patient was discharged from the army in September, 1942.

This young man remained symptomless until October, 1946, when he suddenly developed severe crampy abdominal pain on the right side, and in the suprapubic region which after three days became generalized and necessitated admission on October 20, 1946, to hospital. Examination at that time revealed an emaciated, dehydrated, young man, whose abdomen was distended and tense, with deep tenderness throughout, particularly in the right lower quadrant. The liver was palpably enlarged. On admission the temperature was 100°, pulse 126, respirations 40, white blood count 22,800. Generalized peritonitis was diagnosed and through the use of large doses of penicillin, a Miller-Abbott tube, and careful nursing, the patient slowly recovered. Stool examinations repeatedly revealed occult blood. Sigmoidoscopic examination again revealed multiple polypi, and after two biopsies of benign papillomata, a third polyp revealed adeno-carcinoma.

On December 13, 1946, an exploratory laparotomy was done after it was noted that repeated attacks of diarrhœa and rectal bleeding were painful and debilitating. The liver revealed several large, hard, white masses. Adhesions were present throughout the abdomen. A transverse colostomy was performed. A biopsy specimen from the liver revealed metastatic adenocarcinoma of the liver, primary in gastro-intestinal tract.

The patient gradually became weaker until April 1, 1947, when he was confined to his bed most of the time. He complained of continuous pain in the upper abdomen and chest until May 22, 1947, when he finally died almost 5 years after the diagnosis of carcinoma was first made.

Postmortem examination revealed extensive multiple polyposis of the colon from cæcum to anus; ulcerating carcinomata of the rectosigmoid and polypoid carcinoma of sigmoid colon; massive secondary carcinoma of liver (4,055 gm.); ascites (4,000 c.c.); icterus, hepatogenic, minimal; adhesions of small bowel; adhesions of liver to diaphragm and abdominal wall; secondary anæmia; emaciation.

CASE 2

H.R., a 26-year old twin brother, was operated on in a military hospital in April, 1944, for fistula-in-ano, at which time a sigmoidoscopic examination revealed multiple polyposis of the colon. A polyp excised at that time was negative for malignancy. Due to the extent of the condition the patient was repatriated from overseas and discharged in August, at which time a second polyp was removed and reported as benign. This twin remained symptomless until January, 1946, when diarrhœa and crampy abdominal pain were present for one day, and recurred again in May and June, 1946. These complaints apparently led to an appendectomy in May, 1946.

In January, 1947, this veteran noticed fresh blood in his stools. His physician treated his condition by the cauterization of a few rectal polypi, every week until about April, 1947. At this time he began to have 4 or 5 loose bowel movements daily, occasionally blood stained, and associated with lower abdominal crampy pain.

This young man was then admitted to a D.V.A. hospital, where a sigmoidoscopic examination on May 15, 1947, revealed multiple polypi, and a constriction of the rectum 5 inches above the pectinate line. The biopsy specimens of rectal polypi revealed malignant changes in the glandular structures as well as invasion of the lymphatics and blood vessels at the base of one polyp by undifferentiated epithelial cells, presumably originating in an anaplastic carcinoma at a higher level.

An abdomino-perineal resection was contemplated. A barium enema revealed an annular defect in the rectosigmoid region measuring 7 inches in length, as well as numerous rounded defects presenting the appearance of polypi. Radiographs of the chest, spine, and pelvis were negative, and the condition of the patient was good. On May 29, 1947, a transverse colostomy was performed. At operation a hard mass was palpated in the rectosigmoid colon and extensive involvement of the regional lymph nodes was noted. Polypi removed from the region of the colostomy revealed early malignant changes in the glands without invasion of the stalks. On June 28, 1947, a laparotomy was done, and the primary rectosigmoid mass was filling the pelvis and fixed, and secondary carcinomatous deposits were found in the liver. The patient died on August 3, 1947, about 3 months after the diagnosis of carcinoma was made. Permission for autopsy was not granted.

COMMENT

These two case reports reveal the development of carcinoma in twins, arising from predisposing familial polyposis of the colon. The twins were male, and in their 26th year, when they died within a few months of each other from the advances of metastasizing carcinoma. As far as is known they were considered monovular twins. The family history revealed that the father died of "cancer of the stomach or bowel".

The biological behaviour and the clinical course of malignancy is accurately reflected in the cytology of the malignant growth. In case 1 the malignancy of the gut was an adenocarcinoma, and the clinical course was protracted over 5 years. In case 2 the diagnosis was undifferentiated carcinoma, and the patient was dead in a few months.

SUMMARY

Carcinoma developing in familial polyposis of the colon, in young adult male twins, is reported.

Permission received from Dr. J. A. McFarlane, Director of Surgery, Christie Street Hospital, to publish the above cases, is gratefully acknowledged.

PORTO-HEPATO-OMENTOPEXY IN PORTAL HYPERTENSION*

R. E. McKechnie, M.D.

Vancouver, B.C.

The following report is the description of a new operation used in an attempt to establish a satisfactory collateral circulation in a splenectomized patient suffering from portal hypertension secondary to a cavernous transformation of the portal vein.

The patient was a white, unmarried female, aged 22 years, who, since the age of 9 years, had been having recurring bouts of severe gastro-intestinal hæmorrhage, passing blood both by mouth and by rectum. These episodes recurred once or twice yearly and at times almost exsanguinated her. In October, 1946, the patient had an enlarged spleen removed and a biopsy taken of her liver. The biopsy was reported as showing normal liver.

One month after her splenectomy, the patient had a series of severe gastro-intestinal hæmorrhages. These hæmorrhages recurred in January, February and June, 1947. Each episode was severe and the bleeding recurred over a period of several days. Œsophagoscopy was done in January and œsophageal varices demonstrated and injected with a 5% sodium morrhuate solution without apparent effect on the hæmorrhages.

On the occasion of the last admission, in June, she was almost moribund from the loss of blood. Her condition was improved with multiple blood transfusions and the bleeding finally stopped. On July 9, 1947, the patient was subjected to surgery. The abdomen was opened through an upper right rectus muscle splitting incision and the portal vein area examined. The liver appeared normal. The coronary and pyloric veins were greatly distended. The gastro-hepatic omentum was thickened and œdematous in its right lateral margin and contained several large lymph glands. One of these glands was removed and microscopic study revealed it to have a normal structure.

An attempt was made to demonstrate the portal vein and on opening the gastro-hepatic omentum numerous thin-walled venous sinuses were encountered and these bled profusely. The hæmorrhage was so severe and was stopped with such difficulty that further exploration was not considered advisable. The coronary and pyloric veins were ligated and cut. The greater omentum was then turned upwards and a part of the left inferior margin sutured to the denuded portal vein area where the venous sinusoids had been exposed and ligated. The omentum was also attached to the stumps of the coronary and pyloric veins.

The gallbladder was then removed, the gallbladder bed freshened, the liver incised and the edge of the omentum adjacent to the already fixed omentum buried in the liver and fixed to the raw gallbladder fossa with interrupted sutures. The abdominal wound was then closed and the operation completed.

Follow-up.—On the 6th postoperative day, the patient had a movement containing a small amount of tarry stool. In September, the patient passed a dark stool but she was not certain that it contained blood. Otherwise, the patient has been well.

COMMENT

The operative procedure of porto-hepato-omentopexy has been described in the hope that it may be developed to be of benefit to those portal hypertensive patients where portal or splenic vein shunts are impossible or of no value.

The use of omentum to establish collateral channels is not new. O'Shaughnessy[1] demonstrated the ability of the omentum to supply blood to an ischæmic heart. In the so-called Banti's syndrome, the Talma type of omentopexy was evolved to connect the hypertensive portal circulation with the circulation of the anterior abdominal wall. Pemberton[2] recommends the placing of the omentum in the splenic bed after removal of the spleen for splenic anæmia. He also inserts the omentum to different depths in the lateral abdominal wall and ascribes some of the value of the operation to the establishment of collateral channels via the omentum from the portal system to the parietal vessels, and eventually the caval system.

In the treatment of portal hypertension secondary to portal vein obstruction, it would seem that the establishment of a collateral circulation by the Talma operation or by the Pemberton method would be via long and circuitous venous channels that because of their multiplicity and length would necessarily increase the resistance to blood flow. This increased resistance to blood flow might not permit a reduction of the portal hypertension to a satisfactory level. To avoid this increased resistance, it would seem that the shortest route with the largest collateral bed obtainable would be desirable. In cavernous transformation of the portal vein this route would be ideally from a site just proximal to the portal vein area to a site just distal to the portal vein area and, inasmuch as the portal blood flow is not completely obstructed but only slowed down by the increased resistance of the vascular bed of the numerous venous sinuses, the provision of a few more and perhaps larger collateral vessels may be all that is necessary to relieve the portal hypertension.

The operation described has attempted to relieve the portal hypertension of a patient with cavernous transformation of the portal vein by providing a relatively short bridge of venous channels through the omentum from the proximal portion of the portal area to the distal portion of the portal system in the liver substance. To date, the patient is well and has had no recurrence of gastro-intestinal bleeding.

* Vancouver Medical Clinic, Vancouver, B.C.

REFERENCES

1. O'SHAUGHNESSY, L.: *Brit. J. Surg.*, **23**: 665, 1936.
2. PEMBERTON, J. DE J.: *Surg. Clin. N. Am.*, p. 880, August, 1945.

INTRACARDIAC CATHETERIZATION IN INTERAURICULAR SEPTAL DEFECTS*

A. W. Banghart, M.D. and J. A. Lewis, M.D.

London, Ont.

Though interauricular septal defects represent the commonest form of congenital heart lesion, several features of a patient with this defect recently studied by us seem worthy of note.

The patient, a male of 54 years, entered the hospital on March 29, 1946, for treatment following a paradoxical embolism, producing left homonymous hemianopsia. He had been in good health until 1916 when after minor injuries sustained on military service he had developed transient precordial pain, palpitation and dyspnœa, but had returned to duty. Whilst in hospital after a second wound (of an extremity) he was found to have "pleuropericarditis". Frequent recurrences of his cardiac symptoms occurred and he was invalided home. Since then he has had several hospital admissions for these attacks and has been unable to work. Repeated colds and blood-streaked sputum gave rise to an unsubstantiated diagnosis of tuberculosis. Palpitation, dyspnœa and precordial pain, abnormal fatigue and increasingly impaired exercise tolerance have been the dominant symptoms.

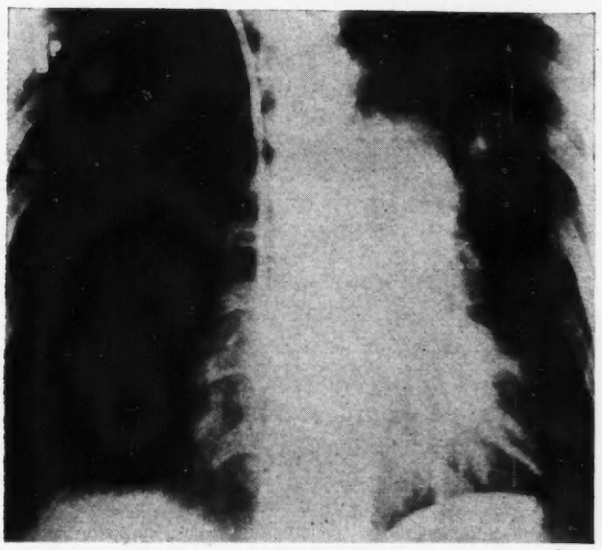


Fig. 1.—Prone position showing catheter in right auricle.

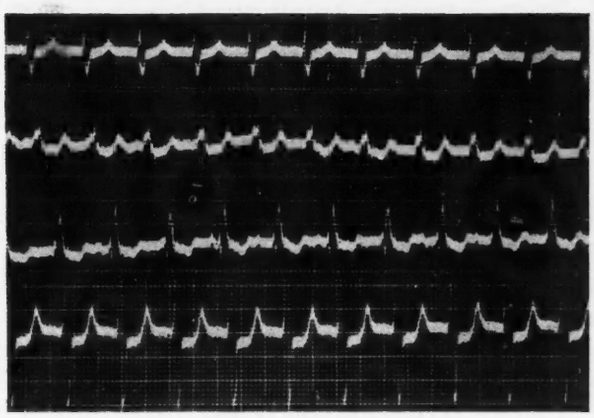


Fig. 2

On admission to our hospital it was found that the heart was enlarged to the right and left, with visible systolic retraction of the 5th left interspace in the area of the cardiac apex. No thrill was felt. At the apex a late diastolic murmur was audible, interpreted by some observers as a split first heart sound. The rate was 104, the rhythm regular, blood pressure in both arms 130/100. The peripheral arteries showed sclerosis in keeping with his age. There was no venous engorgement. Cyanosis was produced by slight exercise. The chest was emphysematous with poor but equal expansion, and a resonant note throughout with cog-wheel breathing. The upper abdomen and lower intercostal spaces "fluttered" at a rate of 96 to 100 per minute, not synchronous with the heart beat. This fluttering disappeared on deep sleep induced by sedation, and was exaggerated by excitement, or breath holding. Fluoroscopic study revealed "flutter" of both leaves of the diaphragm. There was no enlargement of liver or spleen, or ankle œdema. Neurologic examination revealed left homonymous hemianopsia with hyperæsthesia over the left cheek. The left lateral cutaneous nerve projection showed hyperæsthesia. The left thigh movements were weak. These latter findings were related to wounding.

During his stay in hospital repeated attacks of paroxysmal tachycardia, of sudden onset and offset, occurred. During these attacks the apical rate varied between 120 and 140 with venous engorgements and cyanosis but no pulmonary congestion. These attacks were uninfluenced by vagal stimulation but seem rendered less frequent by the administration of quinidine sulfate. No essential change occurred in his general condition whilst under observation. Numerous teleroentgenograms taken from 1929 to the present disclose no change in the cardiothoracic ratio; they show the cardiac configuration which may be found in interauricular septal defect[1] (Fig. 1). Electrocardiogram showed prominent P waves and interventricular conduction delay. During attacks tracings were identical, showing a regular ventricular rhythm. There was an inconstant relationship between P and Q.R.S. suggesting that the tachycardia was ventricular in origin, but there was some disagreement on this (Fig. 2).

Cardiac catheterization was carried out by the method of Cournand.[2] Results of blood oxygen determinations are shown in Table I. Special attention is drawn to the increased oxygen content of right auricular blood as contrasted with caval blood.

TABLE I.

Origin of blood	*Volume % O_2*
Inferior vena cava	15.9
Superior vena cava	15.8
Right auricle	17.3
Right ventricle	17.6

The increase in the O_2 content of the blood of the right auricle over that of the vena cavæ is conclusive proof that there is an interauricular septal defect. Further, if we assume an arterial saturation of 96%, the arterial oxygen content of the patient's blood may be ascertained from the fully oxygenated blood value and we calculate from the above values that 25% of the cardiac output passes through the interauricular septal defect into the lesser circulation.[11]

Interauricular septal defect is the commonest congenital cardiac lesion, Abbott[3] finding it present in 1,000 cases, and as "primary lesion" 76 times. This belongs to the cyanose tardive

* From the Cardiac Clinic, Department of Medicine, Westminster Hospital, London, Ontario.

group, the shunt being from left to right under basal conditions when compensation is present. Cyanosis appears when the shunt is reversed under conditions of physical stress or decompensation. Uhley[4] has shown that this left to right shunt is on a gravitational basis, since the left atrium lies above the right, the septal defect being on the "floor" of the left atrium. The right atrium thus fills by caval flow plus gravitational flow from the left atrium.

The increased blood volume in the pulmonary circuit results in dilatation and hypertrophy of the right atrium and later of the entire right heart and pulmonary arteries. The left heart takes little or no part in the dynamics and remains unchanged. The aorta, owing to decreased blood volume in the greater circulation, is hypoplastic. Should there be an accompanying mitral stenosis (Lutembacher's disease[5]) there is an accentuation of the above pathological change with moderate enlargement of the left atrium.

Cardiac arrhythmias (tachycardia, auricular fibrillation and heart block), in association with interatrial septal defect occur with many times the frequency of any other congenital cardiac anomaly; 75% of cases reported by Roesler[2] and 68% of cases reviewed by Tinney[6] were complicated by chronic valvular disease. This high incidence of chronic valvular disease may well explain the frequency of associated auricular fibrillation with this congenital cardiac disease. Tachycardias of all kinds are frequent. Heart block is not uncommon for there is often interference with the conduction system associated with defects in the septum.

Interatrial septal defect is not incompatible with an average life expectancy. A recent series of 53 cases reported by Bedford, Papp, and Parkinson[7] survived from 30 to 50 years. Many of these cases lead entirely normal lives while others are delicate, poorly developed, possibly due to the hypoplastic aorta and are forced to lead lives of chronic invalidism. Death most frequently results from cardiac decompensation, pulmonary infections, and pulmonary and paradoxical embolism. The presence of valvular disease does not seem to have any effect on the life expectancy. The defect may exist without physical signs and be unrecognized in life.[8] The diagnosis should be suspected in a patient complaining of paroxysmal dyspnœa and cyanosis, where a pulmonary systolic murmur and accentuation of the pulmonary second sound are present. Diagnosis is substantiated by radiographic evidence of hypoplastic aorta, prominent pulmonary artery, enlarged pulsating hilar shadows. The electrocardiogram shows slight to marked right axis deviation and high P waves. The definitive finding of a higher oxygen content of right atrial than of caval blood, in the absence of tricuspid insufficiency may be added.[12, 13]

The diaphragmatic tic is also of interest though a case of diaphragmatic flutter with symptoms suggesting angina has been described.[9] We feel that in our patient the præcordial distress is related to the paroxysmal tachycardia. Most diaphragmatic flutters are apparently sequelæ of encephalitis.[10] In this patient we have been unable to elicit history in keeping with encephalitis.

SUMMARY

A case of interauricular septal defect, with paroxysmal tachycardia, paradoxical embolism and diaphragmatic "flutter" is reported. The finding of a higher blood oxygen content in the right atrial than in the caval blood in the absence of tricuspid insufficiency is suggested as an important diagnostic sign.

We wish to thank Dr. D. W. B. Johnston of the Surgical Division of Westminster Hospital for performing the actual catheterization. We gratefully acknowledge the interest shown and the facilities provided by Dr. C. S. Burton, Research Department, University of Western Ontario, for performing the blood gas analysis, and for the inferences in Table I; and also the co-operation of the X-ray Department, and Dr. Paul Hauch.

REFERENCES

1. ROESLER, H.: *Arch Int. Med.*, **54**: 339, 1934.
2. COURNAND, A.: *Federation Proc.*, **4**: 207, 1945.
3. ABBOTT, M. E.: Atlas of Congenital Heart Disease, 1936.
4. UHLEY, M. H.: *Am. Heart J.*, **24**: 315, 1942.
5. LUTEMBACHER, R.: *Arch. d. mal d. cœur*, **9**: 237, 1916.
6. TINNEY, W. S. JR.: *Arch. Int. Med.*, **561**: 807, 1940.
7. BEDFORD, D. E., PAPP, C. AND PARKINSON, J.: *Brit. Heart J.*, **111**: 37, 1941.
8. ASH, R.: Stroud, W. B., Diagnosis and Treatment of Diseases of the Cardiovascular System, F. A. Davis & Co., Philadelphia, 3rd ed., 1946.
9. WHITEHEAD, R. W., BURNETT AND TANDHAGEN, J. B.: *J. Am. M. Ass.*, **112**: 1237, 1939.
10. SCHEIFLEY, C. H. AND SASLOW, M. S.: *Ann. Int. Med.*, **26**: 129, 1947.
11. BURTON, C. S.: Personal communication.
12. JOHNSON, A. L., WOLLIN, D. G. AND ROSS, J. B.: *Canad. M. A. J.*, **56**: 249, 1947.
13. BRANNON, H. S., WEENS, H. S. AND WARREN, J. V.: *Am. J. M. Sc.*, **210**: 480, 1945.

SPECIAL ARTICLE

THE DANGER OF RIGID PLANNING IN MEDICAL MILITARY ORGANIZATION

H. Godar, M.D.

Bruges, Belgium

Quite recently, an article concerning the activities, past and future, of the Field Surgical Unit, by Dr. Hillsman, appeared in this *Journal*, stressing the point that he "believed it most important that the knowledge we had gained the hard way should not be buried with us", and suggesting that by some compilation of individual experiences, important information might be recorded for future warfare.

At a time when all controversy regarding the retreat of the Belgian Army during the 18-day campaign of 1940, and the subsequent capitulation of King Léopold has died down, when already military experts are guessing the forms of future warfare, it may be of some interest to recapitulate what Belgian medical military authorities had learned by the first World War, and to what extent they had profited by that experience to set up the medical organization of the Belgian Medical Corps in 1939. Let it be stated that this paper only presumes to deal with such a set-up as seen by a medical officer at Army Corps level.

I was attached to an Ambulance Chirurgicale Légère, a unit which can be compared to the Casualty Clearing Station of the British Army, being the first unit at which battle casualties receive major surgical treatment. Basing their judgment on 1914-18 experience, and apparently unaware of the importance of tactical evolutions put to the test in the Spanish, Abyssinian and Polish Campaigns, Belgian Military Headquarters had provided their Light Surgical Ambulances with an all-embracing, heavy and expensive equipment. With the prevailing picture of a more or less stable front-line in view, the Light Surgical Ambulance was to be a spearhead of surgical treatment, a safety valve for rear formations, and, necessarily, a formation not to be constantly shifted from one place to another. To attain this object, the Ambulance was endowed with spacious tents equipped with central heating for temporary hospitalization of casualties, a complete delousing unit, a wooden operating-room complex, and two trailers, one with a complete sterilizing outfit, the other with a complete x-ray outfit. The Ambulance could provide its own electricity. With an impressive array of surgical and hospital equipment, to say nothing of pharmaceutical stores and a frigidaire with Baxter supplies, medical personnel would obviously, it was thought, be in a position to cope with any situation. Three surgical teams of two surgeons, operating room personnel, and stretcher bearers belonging to the universal donor group completed the medical part of the unit, which also included administrative personnel.

Notwithstanding such a remarkable organization, two major problems had not received sufficient attention, or if they had, one never got the impression that such was the case.

The first problem was one of transportation of such a unit. The formation did have, as part of its basic equipment, a certain number of motor vehicles, provided by headquarters, and also an inadequate number of ambulances. But most of the surgical and hospital equipment having been provided during the eight months of mobilization (September, 1939 to May, 1940), these available means of transportation proved to be negligible when the great test of May, 1940 came. Apparently, such a shortcoming was not the sole privilege of our medical unit, for in the first days following invasion of our country by the Nazi blitz-forces, requisitioning of private transportation assumed vast proportions, and as far as our own little unit was concerned, we had to be content with what we could get, *i.e.*, a small number of obsolete lorries and a couple of delivery cars.

A second problem destined to unmask the shortcomings of our organization was the question of liaison. Theoretically, the Belgian telephone net is a very efficient one and should have been able to cope with all our liaison problems, provided it was not put out of use by enemy action. Practically, we found that our contact with headquarters was far from satisfactory, and we were often ignorant of the latest tactical developments, and consequently had to rely to a great extent on personal initiative on the part of our top commanders. Anybody who is familiar with the psychology of regular army officers knows that, only too often, initiative is considered as a quality inversely proportional to promotion. As we had no field telephones (which would have been useless anyhow), no radio equipment, and as events moved too fast to make dispatch-riders practically useful, our orders were of the scantiest nature. It is doubtful, considering the rapidity of the campaign, if they could have been otherwise.

Such was the situation when, on the night of May 9 to 10, 1940, things started moving. Within 48 hours, it became quite clear that with blitzkrieg tactics, the greatest strain would be on surgical units. Medical and military hygiene units, a not-negligible force in the Belgian Army, were practically never put to the test, and many badly needed doctors were bound to inactivity when they might have been most usefully put to work in surgical units. Operations were too swift ever to allow such a switchover.

The 18 days' activity of our Light Surgical Ambulance could be expressed in the blitz-formula: set up, pull down, pull out; set up, pull down, pull out. Needless to say, the majority of our heavy equipment was never set up. In a densely populated country like Belgium, adequate buildings for setting up our unit within a minimum of time could be found round every corner. The tents, the central heating, the operating-room complex remained on the lorries. But the sterilization equipment built on a trailer proved most valuable and was in constant use. Unfortunately, the trailer with the x-ray outfit was demolished in a Stuka attack; its need was sorely felt during ensuing days.

An unforeseen tactical situation brought the strain to its highest. The German break-through at Sedan, and the panzer dash to Abbeville put the Belgian Army with its back to the wall. Consequently, there was no such thing as a "rear-area" left, and within a matter of hours, rear hospital formations were packed with casualties to overflowing, and orders arrived that evacuation had to stop, and that every casualty had to receive all treatment "sur place". Fortunately for the wounded, capitulation put an end to such an impossible situation, and their evacuation to German conquered areas made adequate treatment again possible.

Such an experience, although a short one, has its lesson. It is a matter of some concern to me that the lesson does not seem to have been learnt. Already, one hears of rigid planning of army medical organization for future needs, should they arise. It seems to me that such planning is doomed to failure, as it is impossible, at the present time, to assess what forms future warfare will assume. Will there ever again be such a thing as a "front-line"? Will parachute tactics, atomic weapons, and guided missiles not turn the entire national territory into a blazing inferno? How, in such incertitude, can one speak of traditional hierarchical formula of medical military organization? Does future treatment of war casualties not call for a national mobilization, on the sites where they now stand, of all civilian medical and surgical facilities?

Such seems to me to be one of the lessons of past experience: any medical military organization of today may be obsolete tomorrow. It would not be wise to make any too rigid plans.

13 Rue du Verger.

The dark spaces in the Milky Way, once referred to as coal sacks, are now known to be vast clouds of cosmic matter, dust and gas, cutting off our view of star masses beyond them.

CLINICAL and LABORATORY NOTES

A HISTORICAL NOTE ON REPLACEMENT TRANSFUSION

Alan Brown, M.D.

Toronto, Ont.

In 1925 Dr. A. P. Hart, a senior physician on the Staff of the Hospital for Sick Children and a member of the Department of Pædiatrics of the University of Toronto, published an article in the *Canadian Medical Association Journal* (**51**: 1,008, 1925) entitled "Familial Icterus Gravis of the Newborn and its Treatment".

In this article he states the details of a private patient of his on whom he did a complete replacement transfusion. I believe, according to the literature, that this is the first instance in which such treatment has been employed. This child is now alive and well. I might also add that we used exsanguination transfusions here in 1921 for various conditions. However, the case I have just mentioned is certainly the first instance of the use of a replacement transfusion in the treatment of erythroblastosis fœtalis.

THE MANAGEMENT OF ACUTE PERFORATED APPENDICITIS

Hugh R. C. Norman, M.D., F.R.C.S.(Eng.& C.)

Toronto, Ont.

The present study is based on cases treated in the Toronto Western Hospital in two periods. The first, from July 1936, until July 1941, was investigated by Dr. L. T. Barclay; and the second, from July 1941, until July 1947, will be chiefly dealt with in this presentation. All cases have been on the public or semi-public wards, and have been operated on by the teaching staff or the resident House Surgeons.

From a review of this series it is learned that a significant leucocytosis does not always occur early in acute appendicitis; that fever is not always an early clinical manifestation; that nausea and vomiting are often absent; and that the degree of tenderness may not be convincing. One can seldom anticipate with accuracy the pathological process within the appendix by the preoperative clinical manifestations. Nor can one anticipate the turn that an acute inflammatory process in the appendix may take. The difficulty, in assessing the preoperative pathological condition present in the appendix, has been exemplified, in reviewing acute and perforated appendicitis, by the fact that many cases diagnosed acute were

reported by the pathologist to be, under the microscope, subacute or chonic. In all cases reported in this paper, the clinical and pathological diagnosis is the same.

The perforated appendix with local abscess formation, has been treated conservatively by means of bed rest, fluids by mouth and intravenously and chemotherapy. Most of these patients will respond to therapy and the abscess will gradually disappear; and after several months an appendectomy is performed when the abdomen is quiescent. In some cases the condition progresses, and drainage of the abscess becomes necessary. This group comprises a small proportion of the perforated cases with which we have dealt.

The basic treatment of perforated appendicitis with peritonitis is surgery. The preoperative preparation of the patient is very important, and its extent depends upon the degree of toxicity and dehydration present. In seriously ill patients it is time well spent to attempt a restoration of the chemical balance by intravenous, blood or plasma, before instituting surgery. The anæsthetic of choice is a spinal, and, in some patients, a small dose of pentothal is ideal in allaying the anxiety and restlessness. With this anæsthetic there is minimal disturbance of the patient, and excellent relaxation, which makes the handling of the tissues easy, and reduces the danger of general contamination to a minimum. Cyclopropane and curare, or ether, may also be used.

The incision of choice, in most cases, is a split muscle, if the diagnosis can be made with moderate certainty. In this series there were 58 split muscle, 14 right paramedian, 15 right rectus and three Battle incisions. At operation it is imperative that the tissues be handled with the maximum gentleness. A local process may be made a general one, if one does not adhere to this. Suction is superior to sponging, for the same reason. In almost every case it is possible to remove the appendix; and if the cæcum is not friable, the stump is inverted. Every case, however, stands on its own merits, and in one where the inflammatory process is very marked, and in which removal of the appendix will cause too much trauma and spread of infection, simple drainage may be the wisest procedure.

It is felt that all the infected fluid should be sucked out of the pelvis from the right gutter, as in this way the complications of intraperitoneal abscess and ileus will be reduced to a minimum. Drainage of the peritoneal cavity depends on the surgeon. In this group, 65 were drained with a Penrose drain into the pelvis and along the right gutter. I believe drainage to be the wisest procedure, and have never regretted it. The drains should be left *in situ* for one week, and then withdrawn, an inch each day, until they are out. Stainless steel wire in the external oblique fascia is an aid in preventing postoperative incisional hernia. All cases should be treated as a general peritonitis postoperatively, because the operation may have spread the infection. Fowler's, or semi-Fowler's position, seems to be the most comfortable one. It is important to stress deep breathing, frequent change of position and movement of the limbs, in order to minimize the danger of chest complications, and pelvic or femoral thrombosis, or thrombophlebitis with its serious complication of pulmonary embolus. Morphine gr. 1/4 every four hours, until flatus is passed, is an important adjunct to treatment.

The fluid balance and blood chemistry are controlled by intravenous therapy, and 3,000 to 5,000 c.c. daily of saline, alternating with glucose saline, may be necessary to keep up the balance, and to restore the dehydrated tissues to normal. The amount of fluid necessary can be estimated by accurate intake and output charts. When the blood chlorides are reduced, hypertonic saline will right this. Reduction in the serum globulin and protein levels is restored by plasma, or whole blood transfusions. Amino acids intravenously, in prolonged cases, aid in preventing hypoproteinæmia.

In any case, where respiratory difficulty or cyanosis is present, an oxygen tent or nasal catheters will be useful. In the early postoperative days a rectal tube, and heat to the abdomen, are very comforting.

Over the past six or seven years there have been marked advances in the postoperative care of these patients, which has greatly contributed to the reduction in mortality. For the treatment of the ileus which accompanies peritonitis, the use of the duodenal or Miller-Abbott tube, with continuous suction, has been a routine since 1943 with our cases. A great deal of the distension is due to swallowed air; and with the nasal tube in position, most of this can be eliminated. Small sips of fluids may be given to the patient, and with the tube in the stomach, this is rapidly withdrawn, but the patient has the supreme satisfaction of moistening the mouth and throat. The continuous suction is maintained until the patient expels flatus, and until intestinal sounds are again heard with the stethoscope, and then it may be clamped off for an hour at a time, and fluids by mouth commenced. When fluids are tolerated, the tube is clamped off continuously for 24 hours, and, if no recurrence of vomiting, it may be removed. A small enema may be given, and oil commenced by mouth, when flatus is expelled and sounds are heard.

Another very marked aid, in reducing mortality and morbidity, has been the introduction of chemotherapy. There are two

periods, that of the sulfa drugs, and that of the sulfa drugs with penicillin. We have no series available with the use of streptomycin. In this series sulfathiazole crystals were used intraperitoneally and in the wound, in 59 cases. In 1941 the sulfa drugs were commenced both locally and generally, and in 1945 penicillin was added as well. Since the combined therapy there has been great improvement in the mortality.

The mortality, in the period 1936 to 1941 before sulfa drugs or continuous suction, in 30 cases, was 5 deaths, or 17%. In the period from 1941 to 1943 in which sulfa alone was used, there were 25 cases, with one death, or 4%. From 1943 to 1945 sulfa drugs and continuous suction were used in 29 cases, with 4 deaths, or 13.8%. From 1945 to 1947 sulfa drugs and penicillin and continuous suction were used in 37 cases, with 3 deaths, or 8.1%. Of this latter group two patients, clinically and at post-mortem, were getting over the peritonitis very well, and died of bilateral pneumonia. The general mortality for 91 cases was 8 deaths, or 8.8%. In 1947 there have been no deaths to date.

It has been reported that the mortality of acute appendicitis in a large American city, was 3.54%. In another series, it is stated that in acute appendicitis, one in 183 die; in acute appendicitis with local peritonitis, one in 44 die; and in acute appendicitis with spreading peritonitis, one in 4 die. In 1941 the mortality in the U.S.A. (for perforated appendicitis) was 18%. In our series, from July 1936, to July 1941, there were 336 cases, with 8 deaths; a mortality of 2.4%. From July 1941, to July 1947, there were 330 cases, with eight deaths; a mortality of 2.4%. Excluding the perforated cases, it was found that in 246 cases, there was one death; a mortality of 0.4%. This death was described as due to pulmonary embolus.

There has been a marked improvement in morbidity in the last seven years. The average hospital days, for those cases having sulfa drugs, was 24.4 days; and those having sulfa and penicillin, was 18.7 days. It is to be noted that the more severe cases all had chemotherapy.

CONCLUSIONS

A study of acute perforated appendicitis, in the past eleven years shows that since the introduction of the Wangensteen continuous suction and chemotherapy, the mortality has been halved. Complications have been reduced, and the number of days in hospital have also been greatly reduced. It is imperative that every case of appendicitis be recognized and treated at the earliest possible time.

Medical Arts Bldg.

EXPERIMENTAL USE OF A SKIN-LINED TUBE IN THE GREATER OMENTUM*

(A Preliminary Report)

James R. McCorriston, B.A., M.D., C.M.† and David W. MacKenzie, Jr., M.A., M.D., C.M., D.Sc.(Med.)

From the Experimental Surgical Laboratories, McGill University, Montreal, Que.

In 1946 MacLean and Gerrie[1] reported successful reconstruction of the male urethra by means of a free skin graft in tubular form. Peer and Paddock,[2] and others, observed the fate

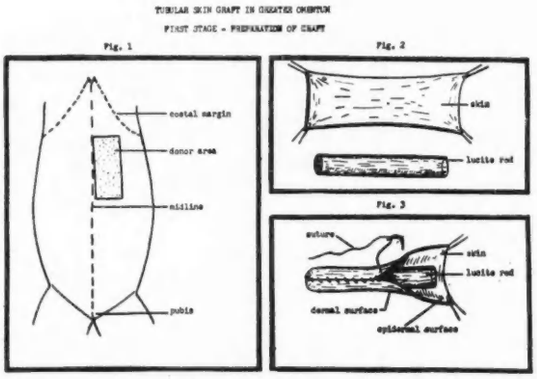


Fig. 1.—First stage operation. Three sketches showing preparation of graft.

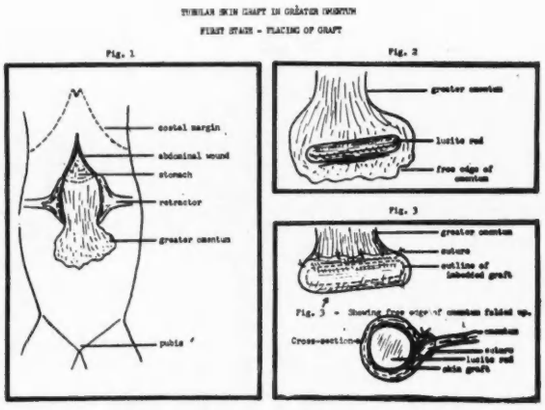


Fig. 2.—First stage operation. Three sketches showing transplantation of prepared graft to greater omentum.

of skin buried beneath the surface of the body. Several surgeons, including Mair,[3] have used skin grafts in the repair of abdominal hernias. These reports show that buried skin survives, and that it resists intermittent exposure to urine. It therefore occurred to one of us (J.R.M.) that skin might also be used for the replacement of otherwise irreparable defects in certain tubular viscera; notably the bile duct,

---

* Presented at the Spring Meeting of the Canadian Society of Clinical Surgeons, April 9, 1948.

† Edward Archibald Fellow in Experimental Surgery.

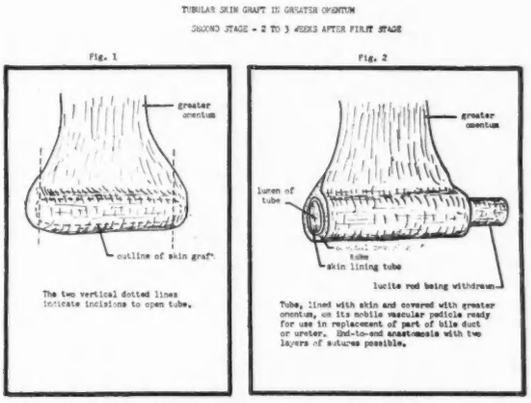


Fig. 3.—Second stage operation. Two sketches showing preparation of skin-lined tube.

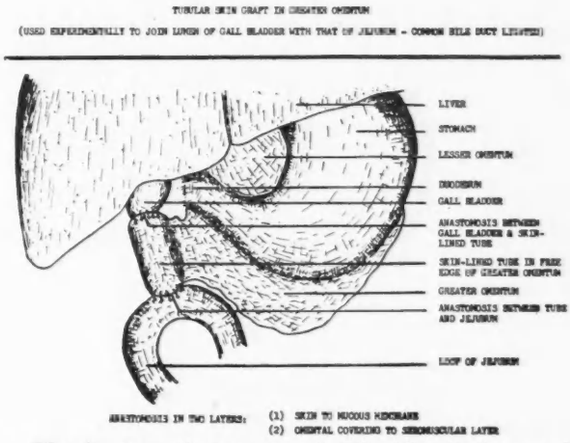


Fig. 4.—Second stage completed. Sketch shows tube connecting gall bladder and jejunum, after ligation of common bile duct distal to cystic duct.

ureter and œsophagus. Accordingly, we decided to implant a skin-lined tube in the free edge of the greater omentum. This site was chosen as a bed for the graft because of its two important characteristics: rich vascularity, and great mobility. It was felt that, once the graft had "taken", it should be possible to swing it into any position in which it might be required to serve as a connecting tube.

METHOD

Free split-thickness and free full-thickness skin grafts were embedded, in tubular form, in the free edge of the greater omentum of rabbits and dogs (Figs. 1 and 2). The condition of the grafts was studied grossly and microscopically at intervals of 11 to 48 days after implantation.

In one rabbit and one dog a pre-formed, skin-lined tube of the above type was used to drain bile from the gall bladder into a proximal loop of jejunum, following ligation of the common bile duct distal to the cystic duct (Figs. 3 and 4).

RESULTS

Free split-thickness and free full-thickness tubular skin grafts survived and acquired a rich vascular supply in the omentum of four rabbits and three dogs. There was no gross evidence of infection caused by the grafts, and only minimal inflammatory cell infiltration and fibrosis were evident in our sections (Figs. 5 and 6).

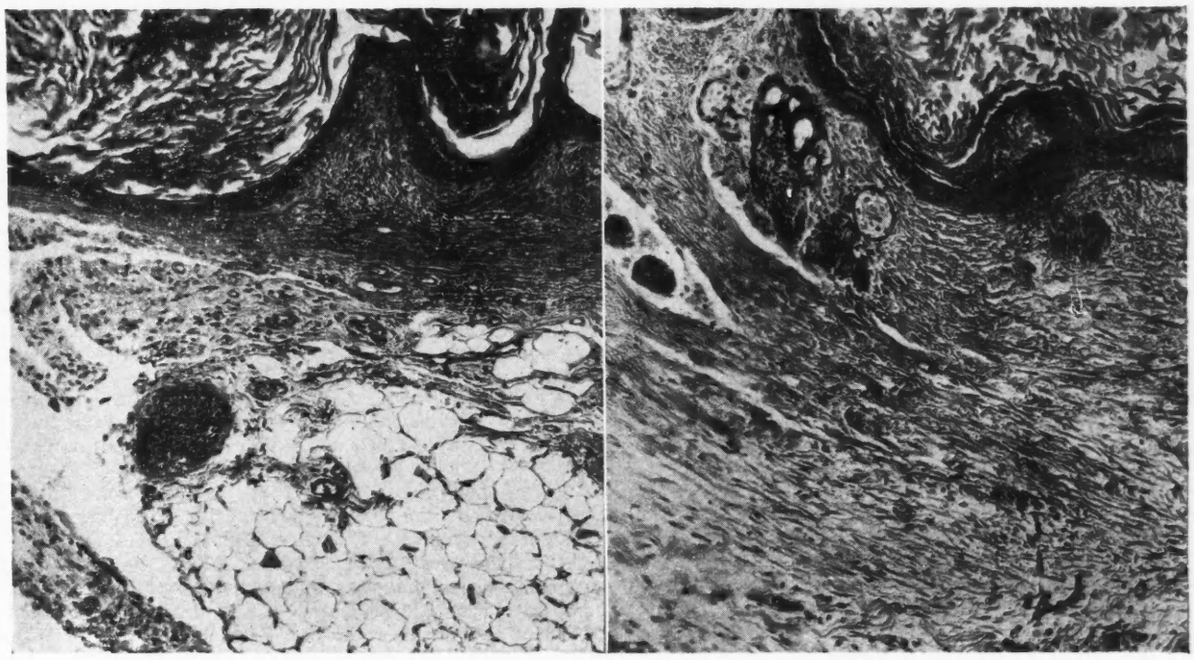


Fig. 5 Fig. 6

Fig. 5.—Part of a cross-section of a tubular split-thickness skin graft in the omentum of a rabbit, 34 days after transplantation. Note vascularity of dermis, absence of inflammatory reaction and survival of epidermis. **Fig. 6.**—Part of a cross-section of a tubular full-thickness skin graft in the omentum of a rabbit, 17 days after transplantation. Note vascularity of dermis and presence of sebaceous glands and hair follicles. Accumulated desquamated material was not removed before sectioning.

The second stage operation, in which bile was drained from the gall bladder into the jejunum, was performed on a rabbit 17 days after implantation of a graft. This animal died on the second postoperative day from bilateral pneumonia. However, autopsy showed that the tube had functioned well and that no leakage had occurred at the suture lines.

The second stage operation was also performed on a dog in the omentum of which a full-thickness tube had been implanted 20 days previously. This animal remained in good health, without evidence of biliary obstruction, until 24 days after operation. It then began to lose weight and, when sacrificed on the twenty-eighth postoperative day, presented definite jaundice. At autopsy, the lumen of the skin tube was found to be about one-half its original diameter (4 mm.). Narrowing was most marked at the mid-portion of the tube. Both sites of anastomosis were patent and complete obstruction of the common duct distal to the cystic duct was confirmed. There was no evidence of bile leakage, but several small biliary concretions were adherent to the muco-cutaneous silk sutures at the jejunal end of the tube.

DISCUSSION

To date, this investigation has shown that, in rabbits and dogs, free tubular skin grafts survive when embedded in the greater omentum; that they heal along their suture lines, retain their structural characteristics and resist prolonged exposure to bile. Infection caused by the skin has not as yet been observed. The omental covering of these tubes provides the advantage of a second, sero-seromuscular, layer of sutures in addition to the muco-cutaneous layer.

It appears that split-thickness are preferable to full-thickness grafts and these should be cut thin in order to exclude the greatest possible amount of elastic tissue and accessory skin structures.

Among the disadvantages of the use of skin within the abdomen is the necessity of a two-stage operation. In certain cases, previous intraperitoneal disease may have seriously reduced the mobility of the greater omentum. Possible complications include infection, fistula formation, compression, stenosis or necrosis of the tube, and the formation of concretions within its lumen.

CONCLUSIONS

Free tubular skin grafts survive when embedded in the greater omentum of dogs and rabbits. At this early stage of our investigation it is possible to say that, in a dog, such a tube (full-thickness) conducted bile satisfactorily for 24 days.

REFERENCES

1. MACLEAN, J. T. AND GERRIE, J. W.: *J. Urol.*, **56**: 485, 1946.
2. PEER, L. A. AND PADDOCK, R.: *Arch. Surg.*, **34**: 268, 1937.
3. MAIR, G. B.: *Am. J. Surg.*, **69**: 352, 1945.

ECONOMIC ASPECTS OF TOBACCO ADDICTION.—At a meeting of the Society for the Study of Addiction on January 20 Mr. Zachary Cope, F.R.C.S., said that tobacco had already achieved an economic status in 1492, when Columbus discovered it in use among the American Indians. The earliest reference to it mentioned the leaves as being bartered for other commodities. By 1523 a tobacco trade had been established in Portugal. Even the calumet, or pipe of peace, was of economic and political importance. The area in which the red stone was mined for making these pipes became sacred, to enable the manufacture of pipes to continue during war, and afforded sanctuary to refugees. Smoking had become so well established in England by 1560 (nearly all the tobacco coming from the West Indies through Spain) that Queen Elizabeth was able to put a duty of 2d. on each lb. Virginia was first successfully colonized in 1607. No money was allowed to be exported from England thither; so the colonists adopted the Indian practice of using tobacco as currency. At first they acquired the tobacco from the Indians, but John Rolfe, who married Pocahontas, started to grow his own tobacco; and soon all the colonists were doing so (manufacturing their own money) to such an extent that a law was passed that no-one should plant tobacco before he had planted 2 acres of corn. By 1639 Virginia produced 1,500,000 lb. of tobacco annually.

This industry had inevitable repercussions on the labour market. When the tobacco farms grew too large for the colonists to manage, they imported indentured apprentices from England; but this made them have to change each employee every five years, which was inconvenient. So black slaves were imported from West Africa, and the tobacco and slave trades rose and flourished together. About 1800 the cotton trade joined these two and detracted somewhat from the tobacco trade. But in 1849 was discovered the light yellow leaf which became so popular that tobacco production was doubled in ten years, becoming indeed of really tremendous economic importance. Next the American civil war crippled the industry by destroying the tobacco farms and liberating the slaves; and recovery was slow. Finally came the war of 1939-45, during which the yearly output of tobacco rose from 1,400,000,000 lb. to 2,300,000,000 lb.

So much for Virginia. What about England? It is said that as early as 1614 there were 7,000 shops in London at which tobacco could be bought. King James, author of the famous *Counterblast to Tobacco*, put on an additional tax of 6s. 8d. a lb. This led the English to emulate John Rolfe and grow their own tobacco, especially in Gloucestershire. Naturally this interfered with the Virginian trade, and the planters protested that their livelihood was being taken from them. So tobacco-growing was banned in England. Troops were used to ferret out the plantations, and a special officer was appointed to suppress them. But it took seventy years to stamp out the practice. The trade with Virginia was used as a cradle for the Royal Navy. By the Navigation Act of 1651 all goods from the colony had to be shipped in either English or colonial ships. A few years later there were 100 vessels engaged in this trade; and on one occasion 300 vessels sailed with the year's crop of tobacco.

At present the annual consumption of tobacco is 5 lb. per caput in the United Kingdom, and 7 lb. in the U.S.A. The tax of 54s. 10d. a lb. in the U.K. now represents an annual tax of £10 per caput of the entire population, or £20 per caput of all adults. The world's production of tobacco is now 7,000,000,000 lb., or 2 lb. per caput of its population. And the wheel has come full circle as regards the use of tobacco as currency, for everyone knows that 200 cigarettes were equivalent to £30-50 in occupied Germany after the war. The difference between the cost price (1s. 2d. a lb.) of tobacco in the U.S.A. and the selling price (£3 a lb.) in the U.K. is an enormous incentive to smuggling.—*The Lancet*, January 31, 1948.

THE CANADIAN MEDICAL ASSOCIATION

Editorial Offices—3640 University Street, Montreal

(Information regarding contributions and advertising will be found on the second page following the reading material.)

PUBLICITY IN MEDICINE

THE medical profession has always been accused of not telling the public enough. Nowadays the accusation can hardly be made in connection with technical matters, as there is nothing in this respect that is hidden from the attention of the lay press. But, with modern developments in the social aspects of medicine new demands have arisen. It is now necessary that the medical profession should constantly make its position clear on what is called medical economics. For the layman the emphasis is mainly on the "economics". He demands, and with justification, that he be not penalized financially for what he cannot help, that is, illness or accident. The physician whose function it is to protect him or if necessary treat him, may feel the injustice of the penalty of illness, and is ready to mitigate it as much as possible. But he realizes that whether illness is inevitable or not, the cost of dealing with it cannot be escaped. It is in trying to make his position in the matter clear that difficulties arise. We all know the questions which are asked. Should compulsory health insurance be introduced? If it is will it provide medical care of as high a standard as under the present system? Should we not rather allow the voluntary health service plans, such as the Blue Cross, to find their level? How shall the doctor be paid, and how much? What about specialist's fees? How shall doctors be distributed to best advantage?

These are a few of the things involved in medical economics. It surely is wise to discuss them with the public, but how to do it is another matter. Should we employ direct methods of publicity to set forth our viewpoint? It is not easy to do that without being told that we are using propaganda. Words are hard masters and that particular term involves unpleasant possibilities. And yet we are an independent profession with high ideals, and we have a right to express our views. Perhaps this best can be done by gradual education, through discussion groups, radio talks, debates, and so on, as asked for. Repetition is a most important element. It is not enough to express our views in medical meetings and journals. No one reading the *British Medical Journal* in these past months can fail to have been impressed by the tremendous outpouring of letters from doctors about the National Health Service Bill; and there must have been very many more in the lay press. And yet even with all this and much more publicity there were those who said that the profession had not presented its case effectively enough to the public. It does not appear to us how much better it could have been done, but it may be that the criticism was directed at its not being done more before the crisis developed. Now we Canada have no such crisis facing us. But we understand that health insurance will again soon become a political issue and education of the public on its implications will be needed. The real business of the physician is to do his work to the best of his ability, but even though explaining himself is a secondary function, and beset with difficulty, it still is of the greatest importance and must be continuously exercised.

EDITORIAL COMMENT

Annual Report of the Montreal General Hospital

The 126th Annual Report of the Montreal General Hospital is worthy of note in more than one respect. The size of the institution and its unsurpassed length of service both as a hospital and a teaching centre give it unusual authority in the hospital field, and its conclusions as given in this report are of more than passing interest. As is the case with many general hospitals the Montreal General Hospital showed a very large deficit for the past year. This is no new thing in the history of the hospital but there is a point beyond which deficits will not be allowed to go. The serious thing is that there is no sign of any public attempt to deal with the matter of hospital deficits, in spite of the sharply rising demands for hospital services. The conclusion reached in this report is that: "It is certain that the voluntary hospital system as we know it in Canada today is in jeopardy". On the other hand no suggestion is made that the problem would be satisfactorily solved by a national health insurance scheme, whereby the voluntary hospitals would lose their autonomy. The suggestion is made rather that attention should be given to overhauling the whole hospital system in Canada along the lines suggested for hospitals in the United States. This involves the use of public funds in the support and expansion of the hospitals, but emphasis is laid on the

extension of hospital insurance plans such as the Blue Cross. It is recognized of course that hospitals are only one element in the whole program of medical care, but they combine many functions which are related to the work of those concerned with the health of the people. It is reports of this nature which serve to underline the difficulties in medical economics.

Addendum

The paper by Dr. Bruce Chown on "A-B-O and Rh Blood Antigens" in the May issue should read, with regard to the Rh reactions of embryo 2, "reacting to the two anti-sera D (Rh_0) and c (Hr′)".

MEN and BOOKS

TOWARDS HUDSON BAY*

George Ramsay, M.D.

London, Ont.

The writer considers it a privilege to have begun his medical career as one of the "Adventurers trading into the precincts of Hudson Bay", and herewith follows the manner of the adventure.

Leaving London within two hours of graduation in early May, 1910, North Bay was reached next morning. Frost heaves in the track, washouts, and a derailment of the train slowed progress so that Cochrane, 480 miles north of Toronto, was not attained till twenty hours later. Diners were not included in standard equipment of trains then, but those who had food shared, and so I experienced the first of many good-neighbour acts in the North Country. During the trip the train stopped at Mileage 222, now Porquis Junction, to let the prospectors of the early Porcupine rush drop off to begin the long trek of twenty or more miles up the Blackhawk River, now made necessary when Father Paraguay turned prospector and blew up the natural dam that had made the river previously navigable. "Blessings on thee little men" was quoted in reverse with added emphasis by every fellow gold seeker who had to make the long portage.

Then came Cochrane and meeting with Dr. Henderson, who could only wish me luck and take the same train to Toronto with his seriously ill wife. While the engine was being turned and coaled he sketched the program that was impending for the next day, exclusive of interludes and emergencies.

With the disappearance of the last car of the departing train I was sure of knowing the full meaning of desolate, both first person singular and in the objective. Never before had I seen a town in the making. The brew was mud and tarpaper shacks, mud and planks for sidewalks, and just more mud everywhere while urgent hammers maintained a night-long chorus of frenzied erection of still more shacks that were fated to be wiped out in the great fire of the next year.

These were not the only pains of travail. An Armenian woman who had come in the same train went into labour the following afternoon with the presentation that of a brow. The text book on obstetrics was in my trunk and there I found assurance that if it were anterior all would be well if it were left alone, for it would itself be converted into an M-A position. This must have been so for the baby was born spontaneously. The stage setting was different from the hospital maternity ward I had known. We got along with a tea kettle, a tin basin, the bed with standard feather-tick coverlet, two unpacked suit cases, from which I secured some linen and baby clothes, with just patient and doctor as dramatis personæ. The husband came in from "up the line" a week later to greet his first born in swaddling clothes, a style of costuming new to the obstetrician and never since seen.

Supplementing this were, in the words of the auctioneer, incidents too numerous to mention; an accident in the steam shovel gang, the priest capsizing his canoe, the visits to hospital(!) and office work in surroundings utterly strange. The young "doc" didn't need rocking to sleep that next night. He had learned one thing, that "doc" was after all not disparagement of position, but rather a term of appreciation.

Two weeks later the chief had returned and I left for "up the line". Rumour had it that illness was rampant among the work gangs and section station men putting up the dumps in the muskeg. A day at the Ground Hog Crossing fifty miles west of Cochrane where the half-mile temporary bridge built by McGuinnis and his carpenter's square and without other calculations or instruments, never ceased to be a matter of wonderment. This was "end of steel" then and so the trek began with initiation into tump line and pack sack and painful research into what the best dressed walking bosses thought useful in shoes and socks. Napoleon might say that an army marches on its stomach, but personal opinion definitely favours elk boots and heavy wollen socks, and this at the price of blisters and wet feet, days on end.

The "doc" was truly a nomad with necessity as the dominating urge to travel, for it was incumbent to reach a new contractor's camp or engineer's station for the next meal. The arrangements on the line then were that the "doc's" board and lodging was "on the house". This happy situation has never since prevailed,

* Prepared for the Historical Section of the Porcupine District Medical Society.

not even in the army. And so, in the course of the sixty-four miles from the Ground Hog to the Kabinogami, one made many friends, and learned that if you were one of them, these frontier folk, whether an immigrant station man, divisional engineer, or big contractor could be counted on never to let you down. I travelled with the mail carrier on foot and generally somewhat in the rear. He was the first Oxford grouper of my experience for he certainly exemplified "sharing" in a very acceptable manner. On one occasion my travelling companion was a Swede walking boss, years older, but with the ability to out-walk anyone in the district. He had me "on the run" very literally.

Medical situations were interesting. The first trip produced a successful Oschner treatment of appendicitis, and the young Italian went "out to the front" to have his abscess drained. Hand and axillary infections with cellulitis and lymphangitis were frequent, and one quickly learned to wait for fluctuation and walling-off, with incision on your next trip through, which is just about the same time as it now takes in hospital—five days for localization without benefit of penicillin. Extractions made one wish for some rudimentary knowledge of dentistry, especially when last molars were the objective. Some long suffering patients might feel afterwards that "'tis better to bear the ills we have than fly to others that we know not of".

Scurvy, or black leg, came to be quite prevalent among the "station" men, foreigners who lived in shacks and baked their own bread and bannocks, and supplemented this with beans, fat pork, prunes, golden syrup and "high wine". I could not blame them for specializing on the latter. The life they lived needed some forgetting. Actually, they could get the same variety of canned stuff that we had in the contractors' camps, and even some of them who did live well, got scurvy. From what I saw of their bread that moulded quickly in its storage underneath the bed I used to wonder if such moulds gave origin to the characteristic pathology of "black leg" with its horrible stench from ulcerated gums.

Imagine how futile it would be to say to a man, "Go home and eat plenty of oranges". Instead we got new potatoes, and after grating them mixed them with canned cream. The first patient pronounced them "Dobra" after many grimaces, and so they should be for it cost a dollar a pound for freighting west on the C.P.R. from North Bay to Missinabi, and from there by canoe down the river of the same name to our main medical post. In any event, we got a chance to do some preventive medicine, for every one who got the least sign of "black leg" came to the camp for our specific, that has not yet become a textbook remedy, though results would certainly warrant its inclusion in the pharmacopœia.

One sidelight was the observation of the extent to which fatigue was an accompaniment of this vitamin deficiency. The tent hospital of twenty beds was taxed with other folk, and the scurvy patients did the decent thing and helped to get wood for the cook house. At first they could barely walk a few rods to carry in a few sticks of wood; and then within a week or ten days they would stack the wood pile before starting back to work. We showed them how we kept food in closed tins and dry, and we had no return cases. In all we must have seen forty such cases. In contrast one of the engineers had been on location the previous year. Their survey party had plenty of lime juice and he said he drank "barrels" of it, and had to be carried out on an improvised stretcher.

You ask about our nurses. Well, we were sixty miles from end of steel so you will appreciate that there just weren't any. At the onset of the season there were three unseasoned doctors, each covering an average of thirty miles of road with an estimated two hundred workmen per mile. Then when typhoid appeared two colleagues got it and went out to the front, one walking forty miles with a temperature of 102° to reach the work train. He was a classmate, so the week that intervened till his arrival at Cochrane and the message came back was more than anxious. Two other doctors got it and went out, so there was left only the writer and a very loyal assistant and orderly. The original source was a carrier in a contractor's camp; in fact, it was the "big boss" himself, and he had an epidemic in his camp the year before. Then a second wave occurred; an influx of new labourers arrived to replace the ones who panicked with the first occurrence of fever. The newcomers were from Cobalt where that year they had a particularly virulent type. These were mainly maritime people and it was among these that the mortalities occurred. Altogether, we had fifty-two cases with eight deaths, and later when I learned the vital statistics of the disease in hospitals in the city, we were consoled. Typhoid inoculation was then unknown as was 606 for syphilis.

My greatest "peeve" was that a Federal official who had been sent up to help, made his report on conditions *in absentia*, at a distance of forty miles, a distance equal to the rail-less interval separating the writer from the consultant. The divisional engineer made a visit with the doctor to the particular camp and closed it reluctantly, for it meant great loss in money to the contractor as well as delay in getting a line through. A very interesting sidelight, was the action of Indians who were camped on the opposite bank of the river. Patients came to the crossing and hailed for a ferry. The Indians quickly got "wise" to what was the illness, and that night struck camp and went back *up* river instead of proceeding as had been their intention *down* river to Moose Factory.

One other interesting experience was a forest fire. A teen-age boy who was to be a "cache" keeper on the furthest west supply "dump" was hiking with me. We left the finest contractor's camp of the district after breakfast, got through to the Kabinogami to pick up a survey party only to find that they had gone. Our return next morning was unforgettable. We got caught between two fires and had to run for it. Eventually we got to the small river and waited, shoulder deep, for the oncoming wall of fire, saw it swing at the last moment away from our refuge and more important too, away from the sod covered "cache" where the dynamite was stored in a root cellar. Several people had been burned, and the camp levelled to the ground. The outward trek of men and horses was on the way and the dazed expression on the face of the contractor, a grand old man who had been very fatherly to the young "doc", is unforgettable.

Our teamster was extensively burned on face, arms and chest when getting the horses out. Him we coated with grease (lard, I think) and faced a journey of thirty-five miles on foot. He was a very brave man, and never once whimpered. He stayed with us for weeks till fit to continue the journey the rest of the way, still on foot.

In summing up the experience I would say that professionally we learned to "do by doing" simply because necessity forced it on us. After an apprenticeship of several months in circumstances where one had to think a problem out unaided except for the few textbooks I returned to hospital internship with a full appreciation of its privileges.

In a larger view we who were the doctors of the wilderness learned the humanities of medicine among a people who had the fortitude of pioneers and the brotherhood of the Northland.

ASSOCIATION NOTES

Defence Medical Association of Canada

On the first page of the Minutes of the 1947 Annual Meeting of the Defence Medical Association there appears a foreword by the retiring President, Major-General C. P. Fenwick, C.B., C.B.E., M.C., E.D., D.D.M.S., First Canadian Army during World War II and later D.G.M.S. (Army) at National Defence Headquarters. Because his message is considered very timely and wise, it is felt that it should be brought to the attention of all Canadian doctors. This is his message:

"The Defence Medical Association has been in existence for a number of years and has contributed greatly, through its efforts, in securing an interest in the war time medical services. Of necessity during war years the Association did not do a great deal of work, as most of its members were on active service either at home or abroad. During the wars of 1914-18 and 1939-45 the Medical Services acquitted themselves extremely well, and I feel that many of the problems which were discussed at meetings of the Defence Medical Association, both locally and at Ottawa, contributed greatly to the efficiency of the service. To those who have served in the Royal Canadian Army Medical Corps, the work done by the Defence Medical Association is well known. To the younger group who have not had such an opportunity, I would like to point out that a good deal can be contributed in peace time through such an Association towards a most efficient service in time of emergency. By the exchange of ideas with those who are interested in the Reserve Medical Corps and in the Active Force, a great deal of good can be accomplished and definite lines of action taken.

"On behalf of the Association I bespeak the active support of medical officers throughout Canada. A strong local group can be of extreme benefit to the national Association by forwarding suggestions and resolutions, by considering problems which affect them locally, and by taking an active interest in the Reserve Medical Corps in each District. I know from experience that the authorities in Ottawa always welcome suggestions from such an Association, and these suggestions are often carried into effect with much benefit to the Service generally.

"The experiences of those who have served in the last war is of great value to the younger members, both in the Active and Reserve Forces, and their interest is also valuable in order that the lessons learned may be passed along to those who have not, up to the present, had an opportunity to see active service.

"What the future holds in the way of peace is still problematical, but we do know that every preparation should be made in order that the Medical Corps can live up to its motto *In Arduis Fidelis* in case of emergency."

We agree entirely with Major-General Fenwick. The Defence Medical Association needs to be strong and active. Whether an ex-M.O. in any of the three services or not, all medical men should show interest in the Reserve Force. This can be done by joining a Medical Reserve Unit and/or becoming a member of one of the twelve branches of the Defence Medical Association. All doctors can contribute to the continued efficiency of the Armed Forces Medical Services in such a way as to avoid the necessity of having to build up from very little should mobilization become necessary, as happened in 1914 and 1939.

At the Seventy-ninth Annual Meeting of the Canadian Medical Association in Toronto on Friday, June 25, 1948, at 2.30 p.m., Brig. H. M. Elder, C.B.E., Chairman of the Executive of the Defence Medical Association and Chairman of the Conference of Defence Associations, will act as Chairman of the meeting of the Armed Forces Medical Section. The panel discussion will cover the following subjects which should prove to be of great interest: (*a*) Medical Problems of Active Warfare. (*b*) Bacteriological Warfare. (*c*) Atomic Warfare. (*d*) Medical Organization, Service and Civilian.

No one should doubt the importance of preparedness of the Medical Services after listening to these discussions.

COL. J. PAUL LAPLANTE,
Ste. Anne's Hospital,
Ste. Anne de Bellevue, Que.,
Honorary Secretary-Treasurer.

SEVENTY-NINTH ANNUAL MEETING
OF THE
Canadian Medical Association
In Conjunction with the
SIXTY-EIGHTH ANNUAL MEETING OF THE ONTARIO DIVISION
TO BE HELD IN THE ROYAL YORK HOTEL, TORONTO
JUNE 21, 22, 23, 24, 25, 1948

President—Dr. F. G. McGuinness, Winnipeg; *President-Elect*—Dr. William Magner, Toronto; *General Secretary*—Dr. T. C. Routley, Toronto; *Assistant Secretary*—Dr. A. D. Kelly, Toronto.

Arrangements for the Seventy-ninth Annual Meeting to be held in Toronto during the week of June 21 are proceeding satisfactorily. General Council will meet on Monday and Tuesday, June 21 and 22. On Tuesday evening, the members of General Council and their wives will be dinner guests of the Ontario Division. A series of Round Table Conferences has been arranged for the mornings of Wednesday, Thursday and Friday from nine until ten-thirty o'clock, to be followed by General Sessions. Sectional Meetings will be held on Wednesday, Thursday and Friday afternoons. The Annual General Meeting will be held on Wednesday evening, June 23, commencing at 8.30 o'clock. On this occasion, the retiring President, Dr. F. G. McGuinness, will hand over the badge of office to his successor, Dr. William Magner.

SCIENTIFIC PROGRAM

Wednesday, June 23

ROUND TABLE CONFERENCES

9.00 - 10.30 a.m.

Anæsthesia

Subject: *Curare.*

Chairman: Dr. Harold R. Griffith, Montreal. Dr. Georges Cousineau, Montreal; Dr. Maurice Legaré, Montreal; Dr. André Pacquet, Montreal; Dr. Roméo Rochette, Montreal; Dr. C. R. Stephens, Montreal.

Dermatology

Subject: *Recent Advances in the Treatment of Skin Diseases.*

Chairman: Dr. Barney Usher, Montreal. Dr. L. P. Ereaux, Montreal; Dr. G. S. Williamson, Ottawa.

Obstetrics and Gynæcology with Medicine

Subject: *Heart Disease in Pregnancy.*

Chairman: Dr. Nelson Henderson, Toronto (Obstetrics). Dr. H. E. Rykert, Toronto (Medicine); Dr. G. F. Strong, Vancouver; Dr. W. Ford Connell, Kingston; Dr. G. R. Brow, Montreal; Dr. W. R. Foote, Montreal.

Surgery with Medicine

Subject: *Biliary Disease.*

Chairman: Dr. F. I. Lewis, Toronto. Dr. Robert Dickson, Toronto; Dr. D. L. C. Bingham, Kingston; Dr. Fred Wigmore, Moose Jaw.

Ophthalmology

Subject: *Toxic Amblyopia.*

Chairman: Dr. Alex. E. MacDonald, Toronto. Dr. Clement McCulloch, Toronto; Dr. R. G. C. Kelly, Toronto.

Pædiatrics

Subject: *Chest X-rays in Children.*

Chairman: Dr. J. D. Munn, Toronto. Dr. P. H. Malcolmson, Edmonton; Dr. D. L. McRae, Montreal; Dr. Adrian Anglin, Toronto; Dr. Gladys Boyd, Toronto.

Psychiatry

Subject: *The Electroencephalogram in Psychiatry.*

Chairman: Dr. G. L. Adamson, Winnipeg. Dr. John Kershman, Montreal; Dr. H. V. Rice, Winnipeg; Dr. J. E. Goodwin, Toronto.

Radiology

Subject: *The Treatment of Carcinoma of the Breast.*

Chairman: Dr. J. W. McKay, Montreal. Dr. S. Jamieson Martin, Montreal; Dr. Jean Bouchard, Montreal; Dr. William Mathews, Montreal; Dr. Vera Peters, Toronto.

Urology

Subject: *Benign Enlargement of the Prostate.*

Chairman: Dr. Robin Pearse, Toronto. Dr. A. I. Willinsky, Toronto; Dr. S. A. MacDonald, Montreal; Dr. C. Aberhart, Toronto; Dr. C. M. Spooner, Toronto.

GENERAL SESSION

Wednesday, June 23

10.45 a.m.

Valedictory Address: Dr. F. G. McGuinness, Winnipeg, President, Canadian Medical Association.

The Lister Lecture: The Practice of Surgery in Canada: Dr. W. E. Gallie, Toronto.

Myasthenia Gravis; with particular reference to its ocular signs and the present status of treatment: Dr. Frank Walsh, Baltimore, Md.

SECTIONAL MEETINGS

Wednesday, June 23

2.30 p.m.

Section of Anæsthesia

Anæsthesia for Bronchoscopy and Œsophagoscopy: Dr. William Butt and Dr. H. W. Boyes, Toronto.

Pain Relief by Nerve Block: Dr. Fernando Hudon, Quebec; Dr. Andre Jacques, Quebec; Dr. Bernard Paradis, Quebec.

Prevention and Treatment of Postoperative Pulmonary Complications by Bronchial Aspiration: Dr. Robert M. Orange, Sudbury.

Intravenous Procaine: Laboratory Investigation, Dr. Shirley A. Fleming, Toronto; Clinical Applications, Dr. R. A. Gordon, Toronto.

Section of Dermatology

The Diagnosis of Fungous Diseases by Laboratory Methods: Dr. Raymond C. Smith, Toronto.

Pruritus Ani: Dr. Donald S. Mitchell, Montreal.

The Treatment of Early Syphilis by a Five-Week Penicillin-Mapharsen-Bismuth Schedule: Dr. Georges Leclerc, Montreal; Dr. Alberic Marin, Montreal; Dr. F. L. Boulais, Montreal; Dr. Adrien Lambert, Montreal; Dr. J. P. Foisy, Montreal.

Results in the Treatment of Syphilis: Dr. E. J. Trow, Toronto; Dr. H. A. Dixon, Toronto; Dr. H. C. Hair, Toronto.

Section of Medicine

The Management of Hæmatemesis and Melæna: Dr. G. Malcolm Brown, Kingston.

Renal and Hepatic Anoxia: Dr. Bryan G. Maegraith, Liverpool, England.

A Follow-up Study of Ex-prisoners of War in the Far East: Dr. Eustace Morin, Quebec.

Endemic Infectious Hepatitis; A Clinical and Metabolic Study: Dr. M. M. Hoffman, Montreal.

Lupus and Vitamin D2: Dr. E. Gaumond, Quebec.

Section of Obstetrics and Gynæcology

The Anæmias of Pregnancy: Dr. J. R. McArthur, Toronto.

Diuretic Effects of Œstrogens Administered in the Last Four Months of Pregnancy: Dr. Elinor F. E. Black, Winnipeg.

The Significance and Management of Fibromyomata Complicating Pregnancy: Dr. A. E. Trites, Vanvouver.

Vaginal vs. Abdominal Hysterectomy: Dr. W. G. Colwell, Halifax.

Endometriosis—Conservative Treatment: Dr. A. E. Mowry, London.

Section of Ophthalmology

Ocular Manifestations of Head Injuries in the War: Dr. Joseph Hill, Toronto.

The Ocular Signs of Malignant Nasopharyngeal Tumours: Dr. Frank Walsh, Baltimore, Md.

Pseudo-Neoplasm (Chronic Lipogranuloma) of the Bony Orbit Caused by Crystalline Foreign Matter (old Hæmatoma): Dr. Stuart Ramsey, Montreal; Dr. H. Wyatt Laws, Montreal; Dr. J. E. Pritchard, Montreal; Dr. Harold Elliott, Montreal.

Ocular Manifestations of Some Intra-cranial Vascular Lesions: Dr. Mark R. Levey, Edmonton.

Section of Pædiatrics

Poliomyelitis, Panel Discussion Pædiatrics with Preventive Medicine: Chairman: Dr. Nelles Silverthorne, Toronto. Dr. S. S. Murray, Vancouver; Dr. Chester B. Stewart, Halifax; Dr. A. J. Rhodes, Toronto; Dr. C. E. VanRooyen, Toronto; Dr. W. T. Mustard, Toronto.

Section of Psychiatry

Psychiatric Progress under D.V.A.—Panel Discussion: Chairman: Dr. William Baillie, Toronto. Dr. Gordon Hutton, Vancouver; Dr. W. M. Musgrove, Winnipeg; Dr. Ernest Goddard, London; Dr. T. E. Dancey, Montreal; Dr. Mary Salter, Toronto; Prof. Wm. Line, Toronto; Dr. A. B. Stokes, Toronto.

The New Psychiatric Therapies—Panel Discussion: Chairman: Dr. J. C. Thomas, Vancouver. Dr. Gilbert Adamson, Winnipeg; Dr. A. E. Davidson, Essondale; Dr. Norman Easton, Dr. L. D. Proctor, Toronto.

Section of Radiology

A Study of Survivals in Hodgkin's Disease, Treated by Radiotherapy: Dr. Vera Peters, Toronto.

The Workings of the Ontario Cancer Foundation's Pilot Clinic at Kingston: Dr. R. C. Burr, Kingston.

Pulmonary Segments—Diagnosis: Dr. D. T. Burke, Toronto.

Beam Direction in X-ray Therapy: Dr. T. A. Watson, Saskatoon.

Section of Surgery

Surgical Procedures in Pulmonary Disease—Panel Discussion: Chairman: Dr. F. G. Kergin, Toronto. Dr. G. F. Skinner, Saint John; Dr. Hugh Coulthard, Weston; Dr. W. A. Oille, Toronto.

The Management of Acute and Chronic Lesions about the Anus—Panel Discussion: Chairman: Dr. James Danis, Toronto. Dr. E. F. Ross, Halifax; Dr. F. A. B. Sheppard, Winnipeg; Dr. C. McG. Gardner, Montreal.

Section of Urology

Carbon Tetrachloride Poisoning with Renal Complications: Dr. E. Laurie Morgan, Dr. J. P. Wyatt, Dr. R. B. Sutherland, Toronto.

Nephroptosis: Dr. E. R. Hall, Vancouver.

Upper Urinary Tract Calculi—Panel Discussion: Chairman: Dr. N. W. Roome, Toronto. Dr. C. L. Gosse, Halifax; Dr. E. R. Hall, Vancouver.

Vesical Neck Syndrome in Women Past Middle Life: Dr. Magnus Seng, Montreal.

Thursday, June 24

ROUND TABLE CONFERENCES

9.00 - 10.30 a.m.

Anæsthesia

Subject: *Pentothal in Combined Anæsthesia.*

Chairman: Dr. Geo. A. Wainright, London. Dr. W. Hardman, London; Dr. H. G. Norry, London; Dr. W. S. Johnston, London; Dr. C. A. Stewart, Chatham.

Dermatology

Subject: *Occupational Dermatitis.*

Chairman: Dr. George B. Sexton, London. Dr. Harold Orr, Edmonton; Dr. Arthur Birt, Winnipeg; Dr. Wm. Garbe, Toronto; Dr. Lemuel Ereaux, Montreal; Dr. C. H. Wilson, Toronto.

Medicine

Subject: *Diabetes.*

Chairman: Dr. R. B. Kerr, Toronto. Dr. A. L. Chute, Toronto; Dr. E. H. Mason, Montreal; Dr. E. M. Watson, London; Dr. Lennox G. Bell, Winnipeg.

Obstetrics and Gynæcology with Radiology

Subject: *Radiology in Obstetrics.*

Chairman: Dr. Richard T. Weaver, Hamilton. Dr. Howard Moloy, New York; Dr. Charles Vaughan, Hamilton; Dr. G. O. Sutherland, Toronto; Dr. Arthur B. Nash, Victoria; Dr. W. R. Foote, Montreal.

Otolaryngology

Subject: *Allergic Rhinitis.*

Chairman: Dr. D. E. S. Wishart, Toronto. Dr. I. H. Erb, Toronto; Dr. William Oille, Toronto; Dr. George C. Snell, Toronto.

Pædiatrics

Subject: *Cœliac Disease.*

Chairman: Dr. J. H. Ebbs, Toronto. Dr. W. O. Stein, Kitchener; Dr. F. W. Wiglesworth, Montreal; Dr. F. W. Jeffrey, Ottawa; Dr. C. K Rowan-Legg, Ottawa.

Psychiatry

Subject: *The Psychiatric Unit in a General Hospital.*

Chairman: Dr. J. Allan Walters, Toronto. Dr. Geo. A. Davidson, Vancouver; Dr. Arthur Doyle, Toronto.

Surgery

Subject: *The Place of Skeletal Traction and Fixation in the Treatment of Fractures.*

Chairman: Dr. R. I. Harris, Toronto. Dr. John R. Naden, Vancouver; Dr. Geo. F. Pennal, Toronto.

Urology

Subject: *Congenital Anomalies of the Upper Urinary Tract.*

Chairman: Dr. Emerson Smith, Montreal. Dr. A. B. Hawthorne, Montreal; Dr. J. T. MacLean, Montreal; Dr. R. M. Wansbrough, Toronto.

GENERAL SESSION

Thursday, June 24

10.45 a.m.

General Practice in the Changing Order: Dr. W. Victor Johnston, Lucknow.

The Physiological Approach to Medical Problems: Dr. Bryan G. Maegraith, Liverpool, England.

What's New in the Treatment of Common Rheumatic Diseases: Dr. Philip S. Hench, Rochester, Minn.

SECTIONAL MEETINGS

Thursday, June 24

2.30 p.m.

Section of Anæsthesia

Symposium—Anæsthesia in Children. (*a*) *Methods and Techniques* (illustrated by coloured moving picture): Dr. C. H. Robson, Toronto. (*b*) *Panel Discussion*: Chairman: Dr. Digby Leigh, Vancouver. Dr. C. R. Stephens, Montreal; Dr. C. H. Robson, Toronto; Dr. C. I. Junkin, Toronto; Dr. R. B. Nichols, Halifax.

Section of Historical Medicine

Antique Amulets of Medical Interest: Dr. T. G. H. Drake, Toronto.

The oldest Hospital in North America—L'Hôtel-Dieu de Quebec, 1639: Dr. Sylvio Leblond, Quebec.

The Medical Services in the North West Rebellion of 1885: Dr. Ross Mitchell, Winnipeg.

The Indians of the Maritime Provinces, Their Diseases and Native Cures: Dr. A. F. VanWart, Fredericton.

Section of Medicine

Ulcerative Colitis: Dr. F. B. Bowman, Hamilton.

Arthritis—Panel Discussion: Chairman: Dr. Wallace Graham, Toronto. Dr. P. S. Hench, Rochester, Minn.; Dr. F. S. Brien, London; Dr. A. W. Bagnall, Vancouver; Dr. L. M. Lockie, Buffalo.

Section of Obstetrics and Gynæcology

Carcinoma of the Vulva: Dr. W. G. Cosbie, Toronto.

Pre- and Post-operative Treatment: Sir William Fletcher Shaw, Manchester, England.

The Prophylaxis and Conservative Treatment of Thrombophlebitis and Phlebothrombosis: Dr. Thomas Primrose, Montreal.

Seminoma of the Ovary: Dr. Léon Gérin-Lajoie, Montreal.

Section of Otolaryngology

Dizziness—Panel Discussion: Chairman: Dr. Frederick A. Cays, Kingston. Dr. J. C. McBroom, Kingston; Dr. G. B. Macpherson, Kingston.

Carcinoma of the Larynx—Panel Discussion: Chairman: Dr. D. H. Ballon, Montreal. Dr. G. E. Tremble, Montreal; Dr. H. E. McHugh, Montreal; Dr. V. Latraverse, Montreal.

Section of Pædiatrics

Tracheo-œsophageal Fistula: Dr. F. R. Wilkinson, Toronto.

Unusual Anæmias in Children: Dr. R. L. Denton, Montreal.

Self-demand Infant Feeding: Dr. C. K. Rowan-Legg, Ottawa.

Resuscitation in Early Infancy: Dr. J. P. Fletcher, Toronto.

Section of Psychiatry

Old Age from the Psychiatric Viewpoint: Dr. A. B. Stokes, Toronto.

Anxiety States: Dr. Ewen Cameron, Montreal.

Depressive Reactions; Their Importance in Clinical Medicine: Dr. R. O. Jones, Halifax.

Experience with Leucotomy at the Provincial Mental Hospital, British Columbia: Dr. Allen Davidson, Essondale; Dr. Frank Turnbull, Vancouver.

Section of Radiology

The Treatment and Prognosis of Carcinoma of the Cervix Uteri: Dr. A. M. Evans, Vancouver.

The Radiological Index in a Survey of Pneumoconiosis: Dr. Jules Gosselin, Quebec.

The Problem of X-ray Check-ups, Management and Technique: Dr. Albert Jutras, Montreal.

Roentgenology in the Management of Acute Intestinal Obstruction: Dr. R. A. Macpherson, Winnipeg.

Section of Surgery

The Treatment of Congenital Club Foot: Dr. Stuart A. Thomson, Toronto.

Reflex Sympathetic Dystrophy: Dr. J. A. Noble, Halifax.

The Rôle of Surgery in Thyroid Disease: Dr. Gordon S. Fahrni, Winnipeg.

The Diagnosis of Chronic Unilateral Enlargement of the Leg: Dr. J. C. Luke, Montreal.

Section of Urology

Renal Tuberculosis in Children: Dr. A. B. Hawthorne and Dr. M. Siminovitch, Montreal.

Carcinoma of the Prostate—Panel Discussion: Chairman: Dr. H. D. Morse, Winnipeg. Dr. E. H. Bensley, Montreal; Dr. Paul Bourgeois, Montreal; Dr. Gordon Ellis, Edmonton.

Solitary Renal Cyst with Hypertension: Dr. J. F. Brunton, Hamilton.

Friday, June 25

ROUND TABLE CONFERENCES

9.00 - 10.30 a.m.

Anæsthesia

Subject: *The Anæsthetist as a Consultant in General Medical Problems.*

Chairman: Dr. F. A. Walton, Winnipeg. Dr. E. H. Watts, Edmonton; Dr. R. J. Fraser, Hamilton; Dr. Alan B. Noble, Kingston; Dr. H. W. Boyes, Toronto; Dr. M. Bowering, Regina.

Industrial Medicine

Subject: *Industrial Medicine and the General Practitioner.*

Chairman: Dr. H. Graham Ross, Montreal. Dr. Angus McKillop, Mimico; Dr. M. F. McGavin, Windsor; Dr. H. Gurth Pretty, Montreal; Dr. Hall McCoy, Montreal; Dr. F. S. Brien, London.

Medicine

Subject: *Drugs in the Treatment of Heart Disease.*

Chairman: Dr. F. C. Hamilton, Toronto. Dr. J. W. Scott, Edmonton; Dr. G. R. Brow, Montreal; Dr. G. F. Strong, Vancouver; Dr. E. A. Bartram, London.

Obstetrics and Gynæcology

Subject: *Early Diagnosis of Carcinoma of the Genital Tract.*

Chairman: Dr. N. W. Philpott, Montreal. Dr. J. E. Ayre, Montreal; Dr. Edwin M. Robertson, Kingston; Dr. Nelson Henderson, Toronto; Dr. W. L. Robinson, Toronto; Dr. Marion Hilliard, Toronto.

Pædiatrics

Subject: *Bowel Obstruction.*

Chairman: Dr. Dudley Ross, Montreal. Dr. J. S. McInnes, Winnipeg; Dr. Stuart Thomson, Toronto; Dr. C. E. Snelling, Toronto.

Psychiatry

Subject: *Psychiatry in Pædiatrics.*

Chairman: Dr. W. A. Hawke, Toronto. Dr. B. H. McNeel, London; Dr. J. D. M. Griffin, Toronto; Dr. E. P. Lewis, Toronto.

Radiology

Subject: *Pulmonary Atelectasis.*

Chairman: Dr. E. H. Shannon, Toronto. Dr. E. A. Broughton, Toronto; Dr. S. L. Alexander, Toronto; Dr. W. G. Carscadden, Toronto.

Surgery

Subject: *Surgical Procedures in the Diabetic Patient.*

Chairman: Dr. W. G. Bigelow, Toronto. Dr. Angus McLachlin, London; Dr. J. C. Luke, Montreal; Dr. Robert Kerr, Toronto.

GENERAL SESSION

Friday, June 25

10.45 a.m.

Mistakes and Pitfalls in General Surgery: Dr. A. T. Bazin, Montreal.

The Scientific Outlook: Sir William Fletcher Shaw, Manchester, England.

Modern Methods of Health Protection in Industry: Dr. C. O. Sappington, Chicago, Ill.

SECTIONAL MEETINGS

Friday, June 25

2.30 p.m.

Armed Forces Medical Section

Panel Discussion—The Newer Medical Problems in the Defence of Canada: Chairman: Dr. H. M. Elder, Montreal.

Medical Problems of Arctic Warfare: Lieut.-Col. J. N. Crawford, Ottawa.

Bacteriological Warfare: Dr. M. H. Brown, Toronto.

Atomic Warfare: Dr. W. R. Franks, Toronto.

The Organization of Medical Research for Defence: Surg.-Capt. A. McCallum, Ottawa; Brig. W. L. Coke, Ottawa; Group Capt. A. A. G. Corbet, Ottawa; Dr. O. M. Solandt, Ottawa.

Section of Historical Medicine

The Food and Medicinal Plants of the Native Indians of British Columbia: Dr. J. H. MacDermot, Vancouver.

Richard Haydock: Being the Account of a Tudor Physician who is also known to History as "The Sleeping Clergyman": Dr. Earle P. Scarlett, Calgary.

Abraham Gesner, Surgeon-Geologist, 1797-1864: Dr. Kenneth A. MacKenzie, Halifax.

Section of Industrial Medicine

Industry—A Medium for the Promotion of Mental Health: Dr. R. G. Bell, Toronto.

Prevailing Practices in Industrial Health Programs: Dr. C. O. Sappington, Chicago, Ill.

The Changing Status of Industrial Medicine: Dr. Harvey Cruikshank, Montreal.

Common Industrial Injuries to the Shoulder: Dr. D. L. C. Bingham, Kingston.

Section of Medicine

The Use and Abuse of Some of the Common Drugs: Dr. M. G. Whillans, Halifax.

Protein Metabolism in Acute and Chronic Illness and Convalescence: Dr. J. S. L. Browne, Montreal.

Diagnostic Bronchoscopy: Dr. C. B. Schoemperlen, Winnipeg.

Hypertension: The Evaluation of Blood Pressure Measurements: Dr. H. N. Segall, Montreal; Dr. J. Siminovitch, Montreal; Dr. S. Barsky, Montreal; Dr. A. M. Vineberg, Montreal.

Section of Obstetrics and Gynæcology

Panel Discussion—Diet in Pregnancy: Chairman: Dr. H. B. VanWyck, Toronto. Dr. E. W. McHenry, Toronto; Dr. F. F. Tisdall, Toronto; Dr. J. H. Ebbs, Toronto; Dr. N. W. Philpott, Montreal; Dr. Ross Mitchell, Winnipeg.

Panel Discussion—Fetal Anoxia: Chairman: Dr. J. F. Puddicombe, Ottawa. Dr. Digby Leigh, Vancouver; Dr. J. F. McCreary, Toronto; Dr. Howard McCart, Toronto; Dr. George White, Saint John.

Section of Pædiatrics

Pædiatric Genetics: Dr. Norma Ford Walker, Toronto.

Bone Diseases in Infancy: Dr. Marcel Langlois, Quebec.

Treatment of Diabetes in Children: Dr. A. L. Chute, Toronto.

Streptomycin in Childhood Tuberculosis: Dr. Gladys Boyd, Toronto.

Section of Preventive Medicine

Are There Nutritional Problems in Canada?: Dr. L. B. Pett, Ottawa.

The Use of B.C.G. Vaccine: Dr. Armand Frappier, Montreal; Dr. Roland Guy, Montreal.

Panel Discussion—Immunization Procedures in General Practice: Chairman: Dr. D. T. Fraser, Toronto. Dr. C. E. Van Rooyen, Toronto; Dr. Nelles Silverthorne, Toronto; Dr. C. D. Farquharson, Toronto; Dr. M. H. Brown, Toronto.

Section of Psychiatry

Insanity as a Legal Defence: The Hon. Chief Justice J. C. McRuer, Toronto. Discussants: Prof. F. C. Auld, Toronto; Dr. G. H. Stevenson, London; Dr. C. B. Farrar, Toronto; Dr. G. F. Boyer, Toronto.

Psychiatric Developments in Saskatchewan: Dr. D. G. McKerracher and Dr. F. S. Lawson, Regina.

Neuropsychiatry and Medicine: Dr. G. W. FitzGerald, Regina.

Section of Surgery

Improved Results in Perforated Peptic Ulcer: Dr. O. W. Niemeier, Hamilton.

Fluid Balance in Surgery: Dr. W. E. M. Mitchell, Victoria.

Diagnosis and Treatment of Mediastinal Tumours: Dr. M. B. Perrin, Winnipeg.

Diagnosis and Management of Scoliosis: Dr. F. P. Dewar, Toronto.

PROVISIONAL LADIES' PROGRAM

Monday, June 21

9.00 a.m.—Registration, Royal York Hotel.

12.30 p.m.—A luncheon for the wives of delegates to General Council has been arranged.

5.30 p.m.—Members of General Council and their wives will be guests of the Academy of Medicine, Toronto, at a reception to be held in the Royal York Hotel.

7.00 p.m.—Dr. and Mrs. Smirle Lawson will entertain the members of general council and their wives at a supper party to be held at their country home, "Idle Hour Farm," Don Mills Road.

Tuesday, June 22

7.00 p.m.—Members of General Council and their wives are guests of the Ontario Division, Canadian Medical Association, at a dinner to be held in the Royal York Hotel. The feature entertainment at this function will be the presentation of the Bell Singers whose appearance is sponsored by the Toronto East Medical Association.

Wednesday, June 23

12.30 p.m.—A luncheon for all ladies attending the meeting will be held at the Auditorium, Eaton's College Street. Following the luncheon a display of the art of the ballet will be presented. Choreography by Miss Mildred Wickson.

8.30 p.m.—The principal evening social event of the Annual Meeting will be the ceremonial installation of the President and the conferring of Senior Memberships. Following this, the newly installed President and Mrs. Magner will receive and the Annual Dance will be held.

Thursday, June 24

5.00 p.m.—His Honour the Lieutenant-Governor of Ontario and Mrs. Ray Lawson will entertain the visiting members of the Association and their ladies at a Garden Party.

8.30 p.m.—Tickets for the concert of the Promenade Symphony Orchestra will be available at the Registration Desk. This event is held at the Varsity Arena, University of Toronto, and although primarily arranged for the entertainment of visiting ladies, any members not otherwise engaged are invited to attend.

Friday, June 25

4.00 p.m.—A Farewell Tea will be held. The location will be announced subsequently. All visiting ladies and Toronto hostesses are invited to be present.

PROVISIONAL PROGRAM OF ENTERTAINMENT FOR MEMBERS

Monday, June 21

5.30 p.m.—Members of General Council and their wives will be guests of the Academy of Medicine, Toronto, at a reception to be held at the Royal York Hotel.

7.00 p.m.—Dr. and Mrs. Smirle Lawson will entertain the members of general council and their wives at a supper party to be held at their country home, "Idle Hour Farm," Don Mills Road.

Tuesday, June 22

7.00 p.m.—Members of General Council and their wives will be guests of the Ontario Division, Canadian Medical Association, at a dinner to be held in the Royal York Hotel. The feature entertainment will be the presentation of the Bell Singers whose appearance is sponsored by the Toronto East Medical Association.

Wednesday, June 23

12.45 p.m.—Association Luncheon.
Guest Speaker—The Honourable Paul Martin, Minister of National Health and Welfare.

8.30 p.m.—Annual General Meeting, ceremonial installation of the President, conferring of Senior Memberships, and the appearance of Delegates from sister medical associations. Following the ceremonial, the newly-installed President and Mrs. Magner will receive, and the Annual Dance will be held. This is the principal evening social event of the meeting and all members and their wives are invited to attend.

Thursday, June 24

12.45 p.m.—Association Luncheon. The program will be in charge of the Ontario Division. All members of the Canadian Medical Association are invited to attend.

5.00 p.m.—His Honour the Lieutenant-Governor of Ontario and Mrs. Ray Lawson will entertain the visiting members of the Association and their wives at a Garden Party.

7.00 p.m.—Alumni Dinners and Class Reunions.
The Medical Alumni Associations of the University of Western Ontario will hold an all-class reunion at dinner in the Tudor Room of the Royal York Hotel.
The Medical Alumni Association of the University of Toronto will hold a dinner at which all members of the Canadian Medical Association will be welcome. The special guests of honour will be the members of the class of 1898 and the class of 1948 University of Toronto. Speaker, L. W. Brockington, Esq., K.C., LL.D.
The Class of 1923 U. of T. will hold its 25th reunion dinner in the Roof Garden, Royal York Hotel. As a special feature, skits reminiscent of Daffydill Nite will be presented at 10 p.m. All members are welcome to attend this portion of the reunion.
The Class of 1928 U. of T. will hold its 20th reunion dinner in P.D.R. 10, Royal York Hotel.
The Class of 1937 U. of T. will hold its 11th reunion at dinner in P.D.R. 9, Royal York Hotel.

Friday, June 25

The Class of 1943, University of Toronto, will hold its 5th reunion dinner at 7 p.m., Friday, June 25, in the Royal York Hotel.

12.45 p.m.—Association Luncheon. Guest speaker, the Honourable Brooke Claxton, Minister of National Defence.

REDUCED FARES FOR RAIL TRAVEL

The Canadian Passenger Association has authorized special convention rates for members of the Canadian Medical Association and their families travelling by rail to the Annual Meeting in Toronto. Identification Certificates permitting members to purchase tickets at a considerable saving may be obtained on application to the General Secretary, Canadian Medical Association, 135 St. Clair Ave. W., Toronto 5.

Dates of Sale

Western Canada—

From British Columbia, June 10-20 inclusive.

From Alberta, June 11-21, inclusive.

From Saskatchewan, June 12-22, inclusive.

From Manitoba and Ontario (Port Arthur, Armstrong and West)—June 13-23, inclusive.

Eastern Canada—

From all points east of Port Arthur and Armstrong —June 13-24, inclusive.

Fare Basis

Round trip tickets will be sold at one and one-third of normal adult one-way first, intermediate or coach class fares, plus 25 cents upon presentation of an Identification Certificate to the ticket agent at the time of purchase of tickets.

Return Limit

Thirty days in addition to date of sale. Passengers must reach original starting point not later than midnight of final return limit.

Golf at the Annual Meeting

Golfers! Dust off your clubs, polish up your game, determine your club handicap and be ready for a round at the Annual Meeting. The Toronto committee in charge of the royal and ancient pastime has arranged for visiting members of the Association to have playing privileges at several of the better local clubs. Friendly matches may be played at any time during the week of June 21, and the Annual Golf Tournament will be held at the Lakeview Golf Club on Thursday, June 24.

The trophies up for annual competition are: the Ontario Cup and miniature to be won by the individual golfer who plays the lowest handicap medal round in the tournament; the Alberta Cup for the best team of four golfers representing any Provincial Division of the Association; for Ontario golfers, the Hamilton Cup for individual medal play; and the London Academy of Medicine Trophy for the best team of four representing a Branch of the O.M.A., will also be played for.

In addition to the trophies, excellent prizes are available for average players. The tournament will get under way early on Thursday to permit visiting golfers to finish in time to accompany their wives to the Lieutenant-Governor's Garden Party, and to attend the many Alumni Reunions being held that evening.

Canadian Urological Association

The program of the Canadian Urological Association, Tuesday, June 22, is as follows:

9.15 to 10.30—Rounds at St. Michael's Hospital, and later at the Toronto General and Toronto Western Hospitals.

3.00 to 4.30—Five papers as follows: *The Place of Perineal Prostatectomy in Urology,* John Balfour, Vancouver, B.C.; *Ureterocele,* J. M. Campbell, Saskatoon, Sask.; *Retropubic Prostatectomy — Advantage and Disadvantages,* C. L. Gosse, Halifax, N.S.; *Diverticulum of the Female Urethra,* Max Ratner and Irwin Ritz, Montreal, Que.; *Streptomycin and Chaulmoogra Oil in Genito-Urinary Tuberculosis,* R. Grant Reid, Montreal, Que.

4.30 to 5.30—Business meeting.

6.30 to 7.30—Dinner, to be arranged.

Canadian Physicians' Fine Art and Camera Salon

The sponsor of this Salon, Frank W. Horner Limited, have received many requests for information. Much effort has been put into making the Salon this year better than ever. More doctors are expected to enter exhibits this year and the response so far has been extremely gratifying. An outstanding jury of selection has agreed to judge the entries this year. The three judges are: Professor K. B. Jackson, B.A.Sc., Director of Photographic Services at the University of Toronto, Mr. A. Y. Jackson, C.M.G., LL.D., one of the original "Group of Seven", and Dr. Harvey Agnew, M.D., F.A.C.P., well-known Canadian physician and artist who has been a frequent winner in past Salon showings.

The Salon will be held in the Royal York Hotel, Toronto, on June 23, 24 and 25 in conjunction with the annual meeting of the Canadian Medical Association. All doctors, whether exhibiting or not, are invited to visit the Salon to see the work of their fellow physicians.

University of Toronto

The Class of 1938, University of Toronto 10th Annual Reunion Dinner, 7 p.m., Royal York Hotel, Hall D. Tickets may be obtained at the Registration Desk.

Canadian Rheumatism Association

The annual business meeting will be held on June 22 at Sunnybrook Hospital at 9.30 a.m. At 10.30 a.m. a clinical meeting will be held with presentation of cases by the staff of the Arthritis Centre. At 2.30 p.m., in private dining room 8, Royal York Hotel, a program of seven scientific papers with discussion will be held.

THE EXHIBITORS

THE LIST of exhibitors for the 79th Annual Meeting is published herewith. Every important aspect of pharmaceuticals and all the varied elements that are required in the practice of medicine and surgery are represented, and we ask that our members make a special point of visiting these exhibits.—(EDITOR).

Cortlandt V. D. Hubbard
Early American Apothecary Shop to be exhibited by Messrs. Smith, Kline & French of Philadelphia.

Abbott Laboratories Ltd.
American Can Co.
American Optical Co.
Ames & Co.
Armour Laboratories
Ayerst, McKenna & Harrison Ltd.

Baxter Laboratories
Becton, Dickinson & Co.
Borden Co. Ltd.
Bristol Laboratories of Canada
British Drug Houses (Canada) Ltd.
Burke Electric & X-ray Co. Ltd.
Burroughs Wellcome & Co.

Camp & Co., S. H.
Canada Starch Co. Ltd.
Canadian Canners Ltd.
Canadian Kodak Co.
Canadian Tampax Corp. Ltd.
Carnation Co. Ltd.
Ciba Co. Ltd.
Coca-Cola Ltd.
Controlite Engineering & Sales Ltd.
Cow & Gate (Canada) Ltd.

Davis & Geck Inc.
Denver Chemical Co.
DeVilbiss Mfg. Co. Ltd.
Dominion Oxygen Co. Ltd.
Down Bros. & Mayer & Phelps Ltd.

Eldorado Mining & Refining Ltd.
Eli Lilly & Co. (Canada) Ltd.

Fisher & Burpe Ltd.
Frosst & Co., Chas. E.

Gerber Products Co.

Chr. Hansen's Laboratory, Inc.
Hanger of Canada Ltd., J. E.
Hartz Co. Ltd., J. E.
Heinz Co. of Canada Ltd., H. J.

Imperial Optical Co.

Lederle Laboratories
Lippincott Co., J. B.

Macmillan Co. of Canada Ltd.
Maltine Co.
Mead Johnson & Co. of Canada Ltd.
Merck & Co. Ltd.

Nestlé's Milk Products (Canada) Ltd.

Ortho Pharmaceutical Corp. (Canada) Ltd.

Parke, Davis & Co. Ltd.
Philips Industries Ltd.
Picker X-Ray of Canada Ltd.
Poulenc Frères du Canada Ltée.

Reckitt & Colman (Canada) Ltd.
Roerig & Co. (Canada) Ltd., J. B.
Rougier Frères Inc.
Ryerson Press

Schering Corp. Ltd.
Sharp & Dohme (Canada) Ltd.
Smith, Kline & French Inter-American Corp.
Smith, & Nephew Ltd.
Spencer Supports (Canada) Ltd.
Squibb & Sons of Canada Ltd., E. R.
Sterne Equipment Co. Ltd.
Stevens & Son Co. Ltd., J.
Swift Canadian Co. Ltd.

Taylor Instrument Co. of Canada Ltd.
University of Toronto Press
U.S. Vitamin Corp.

VanZant & Co.
Victor X-Ray Corp. of Canada Ltd.

Warner & Co. Ltd., Wm. R.
White Laboratories, Inc.
Winthrop-Stearns Inc.
Wyeth & Bro. (Canada) Ltd., John

X-Ray & Radium Industries Ltd.

Zenith Radio Corp. of Canada Ltd.

CORRESPONDENCE

Empire Medical Advisory Bureau

To the Editor:

The Council of the British Medical Association approved the scheme of organization of the above Bureau on October 29, 1947, and have appointed a Committee of Management to organize and develop the Bureau and allotted funds for this purpose. The object of this letter is to inform medical men and women who intend visiting the United Kingdom of the aims of the Bureau, which is housed at B.M.A. headquarters, and the services which it can provide.

One of the main objects of the Bureau is to welcome our overseas visitors from the Dominions and Colonies and make them feel at home in this country. It is hoped to arrange for them to be met on arrival by a fellow-medical at the ports, though this may not always be possible and in any case the visitor is cordially invited to contact the Bureau as soon as possible after arrival in this country and talk over with me any points on which he may need advice or assistance. The Bureau aims at a personal advisory service, which is freely at our visitors' disposal.

The main object of most visitors will be to enlarge their professional knowledge, and detailed information on postgraduate educational facilities and on the courses of study necessary for higher qualifications will be available and, where required, the necessary contacts and introductions will be provided. Visitors who wish to see something of the latest medical and surgical techniques can be put in touch with the appropriate practitioners in these and it is hoped that information on researches being carried out will also be available in due course.

The problem of finding somewhere to live is acute but every endeavour will be made to put visitors in touch with suitable lodgings and hotels. Private hospitality in their homes has been offered by some doctors and it is hoped to develop further this aspect of the scheme.

Information about facilities for sport, travel, theatres, exhibitions, etc., will be available and visitors will thus be able to plan their leisure time as pleasantly as possible.

Ignorance of various important details and regulations concerning food and clothing rationing, petrol allowances, customs duties, etc., may be troublesome and information can be given about these and any other personal matters to enable the visitor to feel at ease as soon as possible in what must be for many a strange land. By social functions and in other ways it is intended to enable practitioners from the Dominions and Colonies to meet each other and prominent members of the profession in this country.

Our visitors may feel there are other ways in which the Bureau can be of service, or other subjects on which they may need advice and I can assure them of our sincere intention to help make their visit to this country both pleasant and profitable.

It will obviously enable the Bureau to be of most service to a visitor if he gives me as long notice as possible of his intended visit and information on the following lines would be useful—projected date of arrival, mode of travel, if accompanied by wife, period of stay, main and other objects of visit and requirements from the Bureau. On arrival, a letter of introduction from the local Hon. Secretary of the Canadian Medical Association, whilst not essential, would be welcome.

It is my intention to send you a quarterly note on current topics and postgraduate training and periodically a summary of postgraduate courses to be held in the United Kingdom.

H. A. SANDIFORD,
Medical Director

Committee of management.—Chairman: Sir Hugh Lett, Bart., K.C.V.O., C.B.E., D.C.L., F.R.C.S., President, British Medical Association. Members: H. Guy Dain, LL.D., M.D., F.R.C.S., Chairman of Council, British Medical Association; J. L. Gilks, C.M.G., F.R.C.S., Chairman, Dominions Committee, B.M.A.; J. A. Pridham, M.C., J.P., M.R.C.S., L.R.C.P., Chairman, International Relations Committee, B.M.A.; L. R. Broster, O.B.E., M.A., D.M., M.Ch., F.R.C.S.; J. Lyle Cameron, M.D., F.R.C.S., F.R.A.C.S., F.R.C.O.G.; Brigadier E. C. Pepper, C.B.E., D.S.O.; A. E. Porritt, C.B.E., M.A., M.Ch., F.R.C.S.; Charles Hill, M.A., M.D., D.P.H., Secretary, British Medical Association. Medical Director, Empire Medical Advisory Bureau, H. A. Sandiford, M.C., M.B., Ch.B., D.P.H.

The Empire Medical Advisory Bureau has been established by the Council of the British Medical Association with a view to giving a welcome and providing a personal advisory service to practitioners visiting the United Kingdom, particularly those from the Dominions and Colonies.

The services of the Bureau will include the following particular objects:

1. To make available the fullest information of facilities for postgraduate study and, where necessary, to provide the necessary contacts and introductions.
2. To maintain a register of suitable lodgings and hotels.
3. To arrange for practitioners from the Dominions and Colonies to be met at the ports.
4. To supply a wide range of general information, including facilities for sport, travel, sight-seeing and entertainment.
5. To arrange private hospitality in doctor's houses.
6. By social functions and otherwise, to enable practitioners from the Dominions and Colonies to meet each other and prominent members of the profession in this country.

The Council of the British Medical Association has appointed the above Committee of Management to organize and develop the Bureau and has allotted funds for this purpose.

The Council has authorized the Committee of Management to establish an Advisory Committee to include full representation of Government Departments and Societies interested in the welfare of Empire and Overseas visitors during their stay in this country for postgraduate education or other purposes.

SPECIAL CORRESPONDENCE

The London Letter

(From our own correspondent)

MR. BEVAN MOVES

At last it looks as if a way were going to be found out of the *impasse* between the profession and the Government which threatened to wreck the whole future of the country's health services. Early in April the Minister of Health announced to the House of Commons that the Government was prepared to make concessions on the three outstanding points of difference between the Government and the medical profession. In the first place he gave an assurance that it would be made statutorily clear that a whole-time service will not be brought in by regulations but would require further legislation to make it possible. With regard to the basic salary, he proposed that this should be compulsory only for new entrants to practice and for the first three years of practice. At the end of this period new entrants will be allowed to decide whether they will carry on with a basic salary or whether they would prefer to forego it and pass to a system of plain capitation fees. Similarly, any doctor already in practice will be allowed to decide whether he wishes to have a basic salary or to be paid entirely by a system of capitation fees. Finally, the Minister has set up an expert legal committee to advise upon the disputed effect of the Act upon partnership agreements.

As soon as these concessions were announced, the British Medical Association decided to hold a new plebiscite to discover the profession's reaction. At the time of writing the result of this plebiscite is not known, but the general expectation is that a majority of the profession will now decide to enter the new service.

THE HEALTH OF THE NATION

At a recent press conference Sir Wilson Jameson, chief medical officer of the Ministry of Health, gave some striking figures concerning the health of the nation during the recent winter. The general death rate for the three months ending March 31 was the lowest ever known in England and Wales: 12.3 deaths per 1,000 of population, compared with over 17 in the corresponding quarter in 1947. During this same period there were only 644 deaths from influenza, compared with 2,796 in 1947 and 4,242 in 1946. The diphtheria figures for 1947 were equally encouraging. For every 10 children who died of diphtheria before the inauguration of the immunization campaign, only one died now. The number of children who developed diphtheria last year was 55,000 fewer than in 1938.

Correspondingly encouraging figures are revealed in the annual report for 1946 of the county medical officer of health for Lancashire, one of the most heavily industrialized areas of the country. The maternal mortality rate was the lowest ever recorded: 1.42 per 1,000 births. The total death rate of 12.61 was 0.51 per 1,000 less than the previous year, and the percentage of deaths under 45 years of age had decreased to less than half of what it was in 1921. That there is no room for complacency is shown by the fact that 1.1% of samples taken of school milk showed the presence of tubercle bacilli, whilst the housing situation is revealed by the fact that 5,300 houses were without adequate internal water supply, and 14,000 had no separate water closet.

SURVEY OF TUBERCULOSIS

In 1934 the Royal College of Physicians of London instituted the Prophit survey of tuberculosis. The report of the first ten years of the survey has just been published and provides some invaluable data on the development and prevention of tuberculosis in young adults. In all, some 10,000 individuals are included in the survey, consisting of contacts, nurses, medical students, naval trainess, and controls. The general conclusions are that young women are more likely to develop tuberculosis than young men, and that risks of exposure in young adults are greater than are generally realized. The risk of developing tuberculosis is in fairly direct proportion to the degree of exposure of the individual to the infection. Although the majority of lesions discovered under observation were minimal, about half become serious enough to require sanatorium treatment. Emphasis is laid upon the necessity for doing more to protect hospital workers and those in contact in families. Although there may be little new in this report, it provides a most useful collection of data which have hitherto been lacking in this country.

CONTROL OF PATENT MEDICINE ADVERTISING

There has just been published by a group of interests including the Newspaper Proprietors' Association and the Advertising Association, a "British Code of Standards in Relation to the Advertising of Medicines and Treatments". This is a further, and welcome, step towards the effective control of the advertising of patent medicines. Newspapers and other advertising media are urged not to accept advertisements which fail to comply with the code, and emphasis is laid upon the fact that the provisions of the code are the minimum standards to be observed. Among the provisions of the code the following are the more important. No advertisement should contain a claim to cure any ailment or symptoms of ill-health, nor should it contain any matter which can be regarded as an offer of a medicine, product or advice relating to the treatment of serious diseases. Appeals to fear are banned, as are offers to diagnose by correspondence. For products offered to women, terms such as "female pills", "not to be used in cases of pregnancy" and "never known to fail" are forbidden. There is also a long list of diseases for which medicines and treatment may not be advertised. These include amenorrhœa, blood pressures, convulsions, dermatitis, sleepiessness, and varicose veins.

To more progressive countries there may not appear to be anything very striking in these recommendations, but it is only fair to point out that they merely epitomize what is already the practice of the more reputable press of this country. Their true significance lies in the fact that they have been put forward voluntarily by the advertising associations of the country.

WILLIAM A. R. THOMSON

London, May, 1948.

A Letter from Australia

[*We are glad to print the following letter from Dr. Wm. C. Gibson, recently on the staff of the Montreal Neurological Institute, who has accepted a post at the University of Sydney. Dr. Gibson's account of the Braund unsavouriness is timely and vigorous. We hope to be able to publish further contributions on Australian affairs.*—EDITOR.]

JOHN BRAUND'S CURE FOR CANCER

On April 9, a Committee of medical practitioners and laymen appointed by the New South Wales Government reported to the State Legislature that the cancer cures claimed by an aged layman, John Braund, were "in no way specific for cancer, nor did they retard the growth of cancer". So concluded a most unhappy chapter of Australian medical history, in which, once again, the hopes of real sufferers from cancer were raised through claims of unreal cures. Patients came to Sydney by air from as far as Vancouver, Canada, only to find an aged charlatan backed by a "Doctor" of physics, injecting alum into patients' bodies, and presenting them with the resultant "slough" as an exorcised cancer.

The committee appointed by the government was most representative, and included not only the Director-General of Health for New South Wales, but several medical nominees, and lay nominees of Mr. Braund. The Leader of the Opposition in the State House was also on the investigating group. They went straight to the matter of examining patients whom Mr. Braund claimed to have cured. At first he indicated that 34 patients had been cured, but as the investigation proceeded it became clear that he had influenced many of them against being either interviewed or examined. In all, 6 patients were examined and the histories of 3 others were obtained.

It became clear that many of the cases did not suffer from cancer, but rather from moles, sebaceous cysts, etc. Mr. Braund felt that special intuition enabled him to diagnose cancer, and he needed no x-rays and no microscope. His ideas of anatomy and physiology were at variance with verifiable facts. The Committee accused Braund of "materially assisting in the death" of cancer sufferers. The similarity between the Braund treatment and the long-since discredited "Roberts cancer cure" and the "Koch-Baker Treatment" was remarked upon. The physicist with Braund, Dr. Brose, had been associated with the latter "cure" in the past. For four years he had been aiding Braund in his phoney therapies also. The committee Chairman, in his summing up, excoriated the layman Brose, for posing as the medical specialist of the team, and charged him with "causing an outstanding public mischief".

The Government Analyst reported that alum in large quantities was recovered from tissue taken from the

breast of one sufferer who had a central slough from a series of peripheral ring-like injections.

The newspaper which reported Braund's amazing "cures" early in the year has been notably silent since the Committee's report has come out. This paper played up the case of a man who was sent home from a hospital with a radiological diagnosis of cancer of the bowel, and who subsequently sought help at Braund's hands. The man's present good health was quickly credited to Braund's ministrations by a layman who heard of it all by the mail, the newspaper got the story and the tragic sequence took on international importance with a vengeance.

One good thing has come out of this sordid chapter, and that is that Mr. E. J. Hallstrom, a Sydney manufacturer who offered Braund £20,000 for a clinic if he could cure cancer, has now given £50,000 to Sydney Hospital for a cancer research fund.

The State Minister for Health, Mr. C. A. Kelly, is wisely considering how best to amend the lax laws of New South Wales which permit unregistered practitioners of any kind to practise as they please, provided that they do not dispense dangerous drugs or sign death certificates. Thus a combination of unsatisfactory legislation, and a lay press shouting the miracle of a supposed recovery from "inoperable cancer" which had been diagnosed at one time and then unfortunately fallen into the hands of a charlatan, set the stage for a chain of events which has cost some patients their homes, possibly some their lives, and all true cancer sufferers another set of blighted hopes.

WM. C. GIBSON

OBITUARIES

Dr. George Chambers Anglin died on April 14 at his home in Toronto.

A native of Ireland, Dr. Anglin came to Canada in 1907 and seven years later graduated in medicine from the University of Toronto. While in London, England, where he was taking postgraduate work, he enlisted with the R.A.M.C., with which he served from 1915 to 1918. During the Second Great War Dr. Anglin was chest consultant for the three services in the Toronto Military District and also for the Norwegian Air Force. He was honoured by the King of Norway with a medal in recognition of his services to the Norwegian fliers. He was a member and elder of Deer Park United Church and formerly active in Y.M.C.A. work, a member of the Senate of the University of Toronto, and several medical organizations.

Surviving are his widow, two sons, two daughters, two brothers and three sisters.

Dr. E. F. Armstrong died recently at his home in Cobalt, Ontario. He is survived by his wife and three sons.

Dr. Frederick W. Blakeman died on April 8 in an Ottawa hospital at the age of 71 years. He was born at Stratford, Ontario.

During the First World War, Dr. Blakeman served in Europe from 1916 to 1918. During the Second World War he was a member of the staff of medical services at national defence headquarters. He retired from the army in 1943 with the rank of major and with the efficiency decoration. A graduate of McGill University in 1904, Dr. Blakeman was a member of the Theta Delta fraternity, a charter member of Defenders Lodge, A.F. & A.M., and a member of the Royal Ottawa Golf Club.

He is survived by his widow.

Dr. William O. Bonser died suddenly at his home in Toledo, Ohio, on April 22. He graduated in medicine from the University of Toronto in 1911. He is survived by his widow, a son, his mother and two sisters.

Dr. Samuel J. N. M. Byers died at Ponoka on April 4. He was born at Bracebridge, Ontario, March 17, 1870. He graduated in medicine from Western University, London, Ontario, in 1899 and commenced his medical practice in Nebraska, U.S.A. where he remained until 1914 when he moved to Rimbey, Alberta. Dr. Byers practised in the Rimbey-Ponoka area until 1944 when he retired from active practice. Evidence of the high esteem in which this pioneer doctor was held was shown in the many beautiful floral tributes sent by individuals and groups, and in the "Tribute" published in the local paper recalling the many sacrifices and hardships endured by Dr. Byers in the early days, and his friendly philosophy and personal interest in the health and welfare of the people he knew so well which endeared him to the hearts of all.

Dr. John Forbes Campbell died in Windsor, Ont., on April 16, after an illness of three months.

A graduate of the University of Toronto medical school in 1905, he practised at Huntsville and Sombra before coming to Windsor in 1913. Dr. Campbell was a former president of the Essex County Medical society and was for a number of years city physician. He is survived by his widow and two daughters.

Dr. John Thomas Courtice died on May 1 in his 72nd year. Dr. Courtice served in the First Great War and held the rank of captain. Since the war he had been associated with Christie St. Hospital. He was born at Clinton and spent his boyhood in the Bay of Quinte district. He graduated from Trinity Medical College in 1906. Surviving are his widow, a son, a sister and a brother.

Dr. A. M. Crawford died on March 24 at his home at Romeo, Michigan, from injuries received in an automobile accident a week earlier. He was 49 years of age. Born at Boissevain, Manitoba, in 1898, he was educated in Vancouver. He served in the Royal Canadian Flying Corps before registering at the University of Alberta in 1920 and attended medical school there until 1922 when he transferred to McGill to complete his studies. He graduated from McGill in 1924. Dr. Crawford practised in Alberta at Mannville from 1924-26; at Westlock from 1926-27, and in Edmonton in 1929-30. In 1930 he moved to New York State where he accepted a post at Mount McGregor Sanatorium. In 1934 he moved to Michigan. At the time of his death he was in private practice, maintaining offices at Mount Clemens and Detroit.

Dr. Crawford won renown as an amateur photographer. Many of his friends value souvenirs of his art. He developed a process of colouring photographs with oils and one of his outstanding achievements in this field was the presentation to parents of coloured photographs of sons serving in the last war. In Dr. Crawford's death, the medical profession has lost a sincere and devoted associate. Humanity has lost a gay and happy spirit whose memory will live on as long as all those who knew him survive. And his research work and writings will keep him alive for many years to come in the profession he loved—the service of his fellowmen. He is survived by his widow, a son and a daughter.

Dr. John Ralston Davidson died in St. Boniface Hospital on April 15 in his 78th year. Born in St. Philippe d'Argenteuil, Quebec, he came west with his parents at the age of seven to a farm in the Manitou district. He graduated in Arts from Manitoba College in 1893 and in Medicine from Manitoba Medical College in 1896. For three years he practised in Morden, then moved to Winnipeg where he practised for nearly fifty years, interrupted only by postgraduate study in New York and Baltimore. In 1905 he was appointed to the honorary attending staff of the Winnipeg General Hospital and served until his resignation in 1930 at the age limit. In 1904 he became associated with the faculty of Manitoba Medical College and from 1913 to 1933 he was Associate Professor of Medicine. He became a

Fellow of the Royal College of Physicians of Canada in 1931. Towards the end of his hospital appointment he was especially interested in the problem of cancer. This led him to undertake experiments with white mice of his own breeding and he was able to produce a strain resistant to tar-carcinoma. He became convinced of the value of injections of embryonic tissue combined with a diet rich in vitamins.

He was President of the old Medico-Chirurgical Society of Winnipeg about 1909, and in 1941 he was made a Life member of the Winnipeg Medical Society, and two years later he was made a Senior member of the Canadian Medical Association. In his younger days he was a fine athlete, excelling as a jumper, and he played on champion lacrosse and football teams. As late as 1927 he played on a medical soccer team on the sports program marking the jubilee of Manitoba University. He is survived by his widow, a son, three daughters and eight grandchildren.

Dr. Harry Glendinning died on April 11 at Wellesley Hospital, Toronto, in his 69th year. He had been ill more than a year. Active in civic and political organizations in Ward 2, Dr. Glendinning served on the Toronto Public Library Board for ten years prior to being elected to the city council as alderman in 1942. He was also a past president of the Progressive Conservative Association.

Medical practitioner in Toronto for 40 years, he was born at Vallentyne, Ont. He attended Markham Collegiate and graduated from Trinity Medical College in 1905. He was a member of the Royal Canadian Yacht Club, Granite Club, Islington Golf Club, King Solomon Lodge, A.F. & A.M.; King Solomon's Chapter, Geoffrey de St. Aldimar Preceptory; Rameses Temple; Enniskillen Orange Lodge, and St. Paul's Anglican Church. Surviving are his widow, two daughters, a son, a sister and a brother.

Dr. Kenneth McKellar Heard, aged 51, died on April 13, at St. Michael's Hospital, Toronto, after a brief illness. He was a member of the Department of Anæsthesia at St. Michael's Hospital, demonstrator in anæsthesia at the University and chairman of the board of governors of the International Anæsthetic Research Society. He was also a past president of the Canadian Anæsthetists' Society and honorary treasurer of the Academy of Medicine.

Dr. Heard was the first to introduce intravenous pentothal anæsthesia into Canada and was also an authority on spinal anæsthesia. In 1941 he organized the Canadian Anæsthetists' Society, serving as secretary and president. Throughout his medical career, Dr. Heard was keenly interested in the welfare of the Academy of Medicine, Toronto, and the Ontario Medical Association. He was chief organizer and promoter of the Academy Telephone Service, serving as chairman from 1938 to 1944, and was instrumental in putting in a pension plan for employees of the academy. He also helped form the anæsthesia section and was chairman for the 1936-37 term.

Born in St. Thomas, where he received his early education, Dr. Heard entered the University of Toronto in 1914. The following year he enlisted and served overseas with the Royal Canadian Corps of Signals. He returned to university after the war and graduated in 1922. He then practised medicine at Iroquois Falls, Ont., until being appointed to the staff of St. Michael's Hospital in 1929. Surviving are his widow and his mother.

Dr. L.-E. Lévesque est décédé le 19 mars à sa résidence à Quebéc à l'âge de 37 ans.

Le Dr Lévesque était bien connu dans le quartier St-Sauveur où il pratiquait depuis plusieurs années. Il était médecin en chef en anæsthésia à l'hôpital de St-François d'Assise. Il laisse sa femme, une fille sa mère, deux sœurs et deux frères.

Dr. James C. Macfarlane died suddenly on March 26 in Westboro, Ont. He was 54 years of age. Dr. Macfarlane, who was born in Ottawa and received his education here, was a veteran of both World Wars, having served from 1914-18 overseas with the Second Infantry Battalion, and from 1939-44 with the Royal Canadian Army Medical Corps. Following the conclusion of World War I, he entered the faculty of medicine of Queen's University, graduating in 1927. He then set up practice in Westboro where he remained until he entered the employ of D.V.A. a few years ago. Dr. Macfarlane was an attendant of Glebe United Church and a member of Ionic Lodge, A.F. & A. M. He is survived by his widow, two sons, one daughter, one brother and two sisters.

Dr. John MacLean, aged 62, died March 18 in Los Angeles. He was born in Glasgow, Scotland, and came to Canada as a boy. He studied medicine at the University of Toronto, and graduated with the degree of M.D. He then moved to Swift Current, Sask., where he practised until the outbreak of the First World War. Being unable to enlist in the C.E.F. because of a disability, he returned to Scotland where he enlisted in the Imperial forces as a medical officer. After serving in France, Dr. MacLean returned to Scotland to study at the University of Edinburgh, and graduated with his F.R.C.S. degree. He returned to Canada, coming to Regina to practise in company with his brother, Dr. Hugh MacLean, until 1924. At that time he moved to Los Angeles where he had practised surgery until his death. He is survived by his widow, one son and two brothers.

Dr. Carl Freeman Messenger, of Middleton, died at the Halifax Infirmary on April 21, after a brief illness, at the age of 43. He was born at Petite Rivière, Lunenburg County, and was educated at Middleton High School, Acadia University, and Dalhousie University, graduating in medicine in 1932. After post-graduate work in New York he settled in Middleton, taking over the practice of his father. Besides carrying on an active and extensive general practice he took an active interest in civic affairs and served as Town Councillor, Chairman of the School Board, and Mayor of Middleton.

Dr. James B. P. Moffatt died on April 13 at Colfax, Wash. He was about 40 years of age. Born in Toronto, he attended Humberside Collegiate, and graduated from the University of Toronto in medicine in 1932. Dr. Moffatt practised in Niagara Falls, Ont., Fort Erie and Long Branch prior to moving to the State of Washington in 1945. Dr. Moffatt served in Canada in the Second Great War as M.O. with the 110th Toronto Squadron, R.C.A.F., and held the rank of squadron leader.

Surviving are his father, a son and a daughter.

Dr. James Howard Moxley died on April 5 in Hamilton. Born in Ottawa on March 5, 1887, he received his early education in that city and graduated in medicine from Queen's University in 1916. After a year of practice in Cobourg, he came to Hamilton and assumed the post of head physician at the Dominion Foundries and Steel Company which he held until the time of his death. In the First Great War he served overseas in the R.C.A.M.C. Dr. Moxley was a member of the Scottish Rite, the Hamilton Club, the Hamilton and District Officers' Institute, and the Hamilton Golf and Country Club. Surviving are his wife, a daughter, and a sister.

Dr. William Robert Patterson, obstetrician and gynæcologist, died on April 20 at his home in Toronto. Born near Kingston, Dr. Patterson graduated in arts from Queen's University in 1903 and in medicine in 1907. After practising for 12 years in Sudbury, he took postgraduate studies in Germany and Austria, and then came to Toronto. A Fellow of the American College of Surgeons, Dr. Patterson was a member of the staff of the Toronto Western Hospital and honorary physician

for St. George's Society. He was active in many organizations and a past president of Toronto Lions Club. He was a 32nd degree Mason and a member of the Æsculapian Club, the Mississauga Golf and Country Club and the Boulevard Club. He was also a member of the board of stewards of Howard Park United Church and the founder and president of the Men's Club of the church. Surviving are his widow and two daughters.

Dr. Walter S. Quint died on April 21, 1948, aged 60, in Rochester Minn. He was radiologist at the Calgary General and the Col. Belcher hospitals, and was a member of the Radiological Association of North America, and The Canadian Society of Radiologists. He served in the 1914-18 war with the R.C.A.M.C..

Dr. John F. Ryan died recently in King's County Hospital, Brooklyn, after a four-month illness at the age of 55. He was a member of the staff of St. Peter's Hospital, Brooklyn. Dr. Ryan was born in Camden, Ont., and graduated in 1915 from Queen's University Medical College in Kingston, Ont. He had practised in Brooklyn since 1925. He is survived by his widow and a brother.

Dr. James Frazer Smith, native of Bornoch, Ont., and first Canadian medical missionary to China, died on April 26. Ninety years old, he had combined medical and theological practice through 60 years. Dr. Smith graduated from Queen's university with both theological and medical degrees in 1888 and after New York postgraduate studies in eye surgery went to China.

He was the first foreigner to set foot in Honan province, to whose Buddhist and Confucian followers he ministered for seven years. Typhus caused his recall and his was one of the first recorded recoveries from the disease.

Dr. George Findlay Stephens, late superintendent of the Royal Victoria Hospital, died on April 29, in his 63rd year. Born in Winnipeg, November 16 1884, Dr. Stephens graduated in medicine from McGill University in 1907, and after some postgraduate work in Europe, began private practice. He served in the war of 1914-18 with the C.A.M.C. and on his return he began his career in hospital administration. His first appointment was as Superintendent of the Winnipeg General Hospital and this he held until 1940 when he became Superintendent of the Royal Victoria Hospital, Montreal. In the same year he was appointed to the Board of Governors of McGill University. He received the Award of Merit of the American Hospital Association for 1946. Dr. Stephen was a pioneer in the Blue Cross plan of group hospitalization and medical care. His interest in Blue Cross began in 1933 when he was president of the American Hospital Association and the first plan to be organized in Canada was with his co-operation in Manitoba. His interest in the Quebec plan began with his arrival at the Royal Victoria Hospital when he found that some groundwork had been accomplished by the Junior Board of Trade.

He is survived by his widow, a son and three daughters.

Dr. James W. Wickware died in March at Madison, Wisc. He was born at Packenham, Ont., in 1872. He attended Carleton Place High School, after which he went west to Manitoba, where he graduated from Manitoba Medical College. He practised his profession in that province for seven years as a pioneer prairie doctor and later in Saskatchewan. Dr. Wickware was a veteran of World War I, serving overseas for some time. At the close of the war he was appointed Pension Examiner for Southern Saskatchewan. After six years he became the District Administrator of Pensions and National Health for Saskatchewan. This position he held until his retirement in 1936. At this time Dr. and Mrs. Wickware moved to Aylmer, Ont., where Dr. Wickware took a very active interest in the life of the community and made a host of friends. He was a member of the United Church of Canada, the Masonic Lodge, being a 32nd Degree Mason, the Canadian Order of Foresters, and the Canadian Legion. He is survived by his widow and one daughter.

NEWS ITEMS

Alberta

At the recent meeting of the American College of Physicians in San Francisco, Dr. Kenneth A. Hamilton received his F.A.C.P. degree. Dr. Hamilton is the Director of Medicine at the Mewburn Hospital, D.V.A. in Edmonton.

Dr. C. W. Stephens of Vermilion, has returned from Chicago where he completed a course in Surgery at the Cook County Graduate School of Medicine.

Dr. L. Weatherwilt, of Lamont, arrived from Vancouver where he attended the D.V.A. hospital for a time.

Dr. Morton Hall, Sr., Pathologist to the Royal Alexandra Hospital is on a tour of the Pathological departments of the hospitals of Stockholm, Sweden and London, Eng.

Dr. John W. Bridge succeeds Dr. E. A. Braithwaite as Chief Coroner for the Province of Alberta.

Dr. E. K. Wright of Athabaska attended surgical clinics in Edmonton of recent date.

Dr. C. B. Rich of Edmonton is leaving for England and while there will take a special course in Cardiology in London. Dr. Rich is a graduate of St. Marys Hospital, Paddington and has practised in Edmonton since 1937. He was with the R.C.A.M.C. during the war.

Dr. Richard N. W. Shillington, Medical Officer in charge of the Veteran Convalescent Hospital in Calgary, retires after giving excellent service to that institution. Dr. Shillington was a former Associate of the late Col. F. H. Mewburn in 1921.

A meeting of the Directors of Medical Services (Alberta) Incorporated, was held in Edmonton on April 14, 1948. Dr. A. E. Archer of Lamont, was named chairman; Dr. R. L. Anderson of Edmonton, vice-chairman and Mr. W. F. Empey of Edmonton, secretary-treasurer. The board hopes to be able to offer prepaid medical care on a group basis to the people of Alberta by early summer. The response from the medical men in signifying their intention to become professional members has been very great.

At the 1948 session of the Alberta Legislature the Associated Hospitals of Alberta incorporated, and with the incorporation obtained power to provide for hospitalization on a prepayment basis and for the sole right in the Province of Alberta to the use of the words "Blue Cross Plan". The Blue Cross Plan will be administered by a board of nine representing various groups of hospitals, the subscribers, municipalities and the College of Physicians and Surgeons.

The following have registered with the College of Physicians and Surgeons, Province of Alberta, since the first of the year: Drs. Eli Abramson, Leslie Christie Allan, Donald Park Beckett, Harvey Hugh deBurgh Black, Thomas Michael Brown, James Harold Herbert Chataway, William LeGrande Cooper, John David Duffin, Donald Armstrong Gibson, Ronald Meredith Jackson, Leon Komar, Alexander Gray McLaren, Brendan Joseph O'Sullivan, Stephen Benedict Thorson, Roland Watson and Nicholas Frederick Wishlow.

A meeting of the Medical Staff of Red Deer Municipal Hospital was held recently with the Hospital Board. Plans for much greater hospital space and facilities were discussed.

Dr. L. J. Patterson, formerly of Prescott, Ontario, has joined The Parsons Clinic in Red Deer.

Dr. J. Mitchell, formerly of Winnipeg, has joined the Red Deer Associate Clinic.

Dr. W. B. Parsons has attended the meeting of the Northwest Pacific Society of Radiologists at Vancouver, B.C.

Dr. J. A. Weddell spent two weeks in Toronto in refresher work in recent months.

Dr. Richardson as our District Representative to the Council of the Alberta College of Physicians and Surgeons presented a brief review of the history and progress towards the Voluntary Health Insurance proposal for Alberta. He discussed the Act to incorporate the Alberta Medical Services Limited in some detail.

A brief report from Dr. A. E. Wilson as President of the Alberta Division of the C.M.A. was given. The annual meeting of the Alberta Division of the C.M.A. would be held September 22, 23, and 24, at the Palliser Hotel. Dr. Wilson also presented a notice of motion which would incorporate the Calgary District Society with the Calgary Society. This motion will be voted upon at the next meeting.

The Secretary was advised that an official vote of appreciation had been forwarded to the Colonel Belcher Hospital for their kind service in using their auditorium.

The motion was made by Dr. Morgan and seconded by Dr. Gelfand that the President and the Treasurer be authorized to sign cheques and handle monies of the Society.

A motion was made by Dr. G. R. Johnson and seconded by Dr. A. I. Danks, that a hearty vote of thanks be tendered to all the officers of the Calgary Medical Society, Inc., for their work in connection with the Society's affairs during the past year. L. M. FAIRBAIRN

British Columbia

The new compulsory hospital insurance bill, referred to previously as having been introduced by the British Columbia Government at the present session of the Legislature, has become law, and will be put into effect as soon as possible. A maximum of $33 yearly will cover all members of a family. There is no limitation on length of stay in hospital. Old age pensioners and others under the social assistance system will be paid for by the Government. Coverage will be complete as to hospital services. Christian scientists, and those already covered by adequate Hospital Insurance schemes are exempted. Regulations are now in process of preparation.

The Vancouver General Hospital reports 4,834 births in 1947. This is believed one of the highest for any general hospital in the world. A new 12-crib nursery for premature babies is being built at a cost of $7,000.

The Government of British Columbia has decided to establish a psychological clinic at Essondale, to "screen" new mental patients. Dr. Clarence M. Hincks, Chief Director of the National Committee on Mental Hygiene said that the clinic may return 70% of the patients to their homes. He urged "home" treatment wherever possible.

Health Units in British Columbia announce some new appointments. Dr. Helen Zeman is the new Director of the Okanagan Health Unit. She is a graduate of the University of Saskatchewan in Arts, and of the University of Toronto in Medicine. She served in the R.C.A.M.C., from 1944 on; then joined the Provincial Department of Health in 1946. She succeeds Dr. A. N. Beattie who has taken charge of the Central Vancouver Island Health Unit.

A new General Hospital for Fernie, B.C., to cost $228,000 is now under construction. It is scheduled to be completed within a year. White Rock, British Columbia, will also have a new 35 bed hospital by Christmas, if all goes well. The Dominion Order of Sisters from Everett, Washington, have offered to furnish and equip the hospital—also to staff and operate it. The Provincial Government will share with White Rock and the Sisterhood, the costs of construction.

Forty-three condidates are writing the Dominion Council Examinations in British Columbia this month. Some of these are from foreign countries. This is a record number for British Columbia.

A tragic pilgrimage came to end recently when three sufferers from inoperable cancer, two women and one man, returned to Vancouver from their trip to Sydney, Australia, whither they had gone to see one John Braund, who claimed to have a cure for cancer. This man has been thoroughly investigated by the authorities in Australia, who pronounce his supposed cure a fraud and without any scientific foundation. The whole episode received a great deal of publicity in the newspapers, and is greatly to be deplored. One cannot but feel regret that so much sensational publicity was given to this man in the press, without any adequate attempt at assessment of the value or worthlessness of his claims. Such awakening of false hopes, by ill-advised journalism, cannot but do harm.* J. H. MACDERMOT

Manitoba

A diagnostic clinic opened in Selkirk General Hospital on May 1, with facilities equal to those of Winnipeg hospitals.

Dr. W. F. Tisdale, Winnipeg, has been elected president of Ducks Unlimited (Canada) which has as its object the conservation of game birds.

Dr. Max Wintrobe, a former Manitoba graduate, now Professor of Medicine of the University of Utah, will address the Winnipeg Medical Society on May 12.

Work will begin shortly on the erection of a Red Cross building on Memorial Boulevard which will house the blood bank and Red Cross offices. The Provincial Government is making a large donation towards the cost of the building.

Manitoba is suffering from extensive floods. In Winnipeg and St. Boniface dykes have been thrown up to protect the Municipal hospitals, King George and King Edward, and St. Boniface Hospital, St. Boniface Sanatorium and Concordia Hospital, all on the banks of the Red River. At Morris, Manitoba, the hospital was closed and patients transferred to a hotel or to Winnipeg. Emerson, on the United States border was almost all under water, as were many small towns along the Red. With the Assiniboine and Minnedosa rivers now on the rampage, the towns and cities of western Manitoba are suffering from flood damage. The Red Cross is giving valuable aid to flood victims and the Department of Health is urging vaccination against typhoid.
ROSS MITCHELL

* See also letter from our Australian Correspondent in this issue.—EDITOR.

Nova Scotia

On April 28, the Halifax Medical Society was host to two of its members at a banquet in the Nova Scotian Hotel. Dr. H. A. Payzant of Dartmouth was celebrating his fifty-first year in the practice of medicine, and Dr. G. G. Gandier also of Dartmouth, his fiftieth.

Dr. Payzant graduated from Dalhousie University in 1897. After practising at Liscomb for a time he came to Dartmouth. During the whole of his professional life he has been a general practitioner. For more than thirty years he has been Medical Health Officer of his town and responsible for an active and progressive public health service. He is a Past President of the Halifax Medical Society. Dr. Gandier, born in Ontario, also graduated from Dalhousie University, but one year later. Following postgraduate studies in England he began general practice in Pictou, Nova Scotia. Later he returned to England for further work and on his return came to Dartmouth, where since 1904 he has specialized in diseases of the eye, ear, nose and throat. Both physicians are highly regarded by the profession in Nova Scotia as ethical and skilful practitioners.

Dr. George H. Murphy, Jr., of Halifax, has been appointed Pathologist and Director of Laboratories at the Winchester Memorial Hospital, Winchester, Virginia.

Following graduation from Dalhousie University in 1940, Dr. Murphy was awarded a Fellowship with the Mayo Foundation in pathology. He interrupted his work there to join the R.C.A.M.C., and during the European Campaign was in charge of a mobile laboratory unit in the forward areas. Returning to his work at the Mayo Clinic he has just received his degree of Master of Science in Pathology from the University of Minnesota, and the Diploma of the American Board of Pathology.

The Victoria General Hospital, Halifax, has announced the appointment of Dr. Robert Murray MacDonald and Dr. Lea Chapman Steeves as assistant attending physicians.

Dr. J. L. Akin, a native of Windsor who has been pursuing graduate work in Montreal will shortly begin practice in his home town.

H. L. SCAMMELL

New Brunswick

Dr. B. E. Pothier of Dalhousie, has returned to his practice after postgraduate study in New York.

Hon. Dr. F. A. McGrand, called a special meeting of the physicians and technical staff of the Department of Health, under the chairmanship of Dr. J. A. Melanson, at Fredericton, to review last year's work and to advance planning for next fiscal year.

Dr. C. L. Gass, of Sackville, was elected President of the Mental Hygiene Council of New Brunswick, at the annual meeting of the organization held in Saint John, recently.

Dr. A. E. Macaulay, has been confined to his home for some time, with an acute illness. Improvement in his condition is reported.

Dr. J. A. Melanson, chief medical officer of the New Brunswick Department of Health, has left for Europe as one of a five man delegation from Canada, to the meeting of the World Health Organization. On the agenda of this meeting is the ten year review of statistical services and nomenclature of Causes of Death.

The Cancer Diagnostic centre at Moncton City Hospital is to open soon, Dr. J. W. Dobson is clinician in charge and Dr. J. B. Stewart is the alternate.

Dr. Vincent J. Sadovsky, until recently practising in Saint John, has accepted a position in Hurst, Ontario.

Dr. D. A. MacLennan, and Dr. J. P. Carette, were appointed clinician to the Cancer Diagnostic Clinic at Campbellton, which will be organized at the Hospital Hotel Dieu.

Dr. Geo. F. Skinner, of Saint John, has been appointed an Examiner in Surgery on the Certification Board of the Royal College of Physicians and Surgeons of Canada.

Dr. J. J. MacPherson, heads a committee in an effort to collect $250,000.00 as a building fund to extend facilities of the Soldiers' Memorial Hospital at Campbellton.

Dr. J. K. Sullivan and Dr. J. P. McInerney of the Urological and Surgical Staff of the Saint John General Hospital, are at present taking postgraduate study at the New York Cancer Memorial Hospital.

A. STANLEY KIRKLAND

Ontario

Dr. F. Tisdall has been given the signal distinction of Fellowship in the Royal College of Physicians. This recognition of the outstanding work of Dr. Tisdall in the field of nutrition is greatly appreciated by his colleagues and his many admirers and friends in the profession.

Dr. C. H. Best, Professor of Physiology, University of Toronto, delivered the annual Phi Beta Pi lecture at Baylor University College of Medicine, Houston, Texas, on March 22. He spent the remainder of the week as visiting Professor in the Department of Physiology.

Dr. Ray F. Farquarson Professor of Medicine, University of Toronto, spent a week in April as acting physician-in-chief at Vancouver General Hospital.

The Toronto Diabetes Association was formed on April 29, 1948. The object of this association is the improvement in the treatment of diabetes mellitus through study of the disease, dissemination of information concerning it, or by any other means. The following are the officers: *President*—Dr. C. H. Best; *Vice-president*—Dr. R. B. Kerr; *Secretary*—Dr. A. L. Chute; *Treasurer*—Dr. L. A. Chase; *Members of Council*—Drs. R. Haist, Walter Campbell, W. E. Hall.

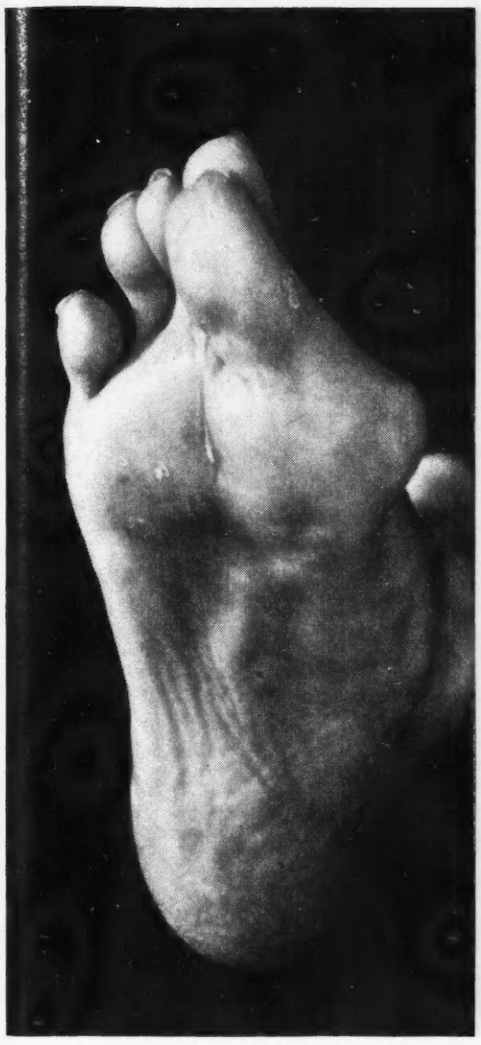
A. A. Epstein, M.D., C.M., D.Rad., has announced the opening of his office at 394 Bloor Street West, Toronto, for the practice of Diagnostic and Therapeutic Radiology.

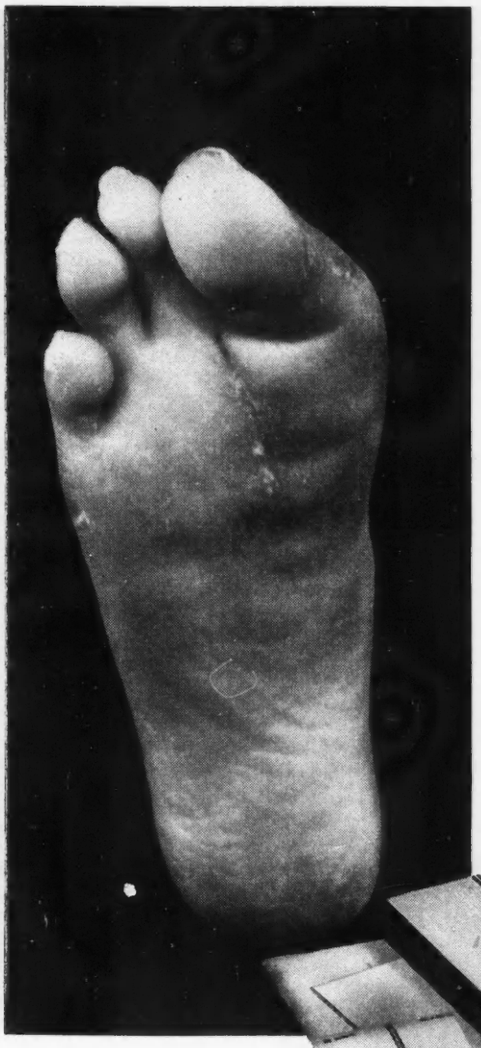
Toronto is to get Chorley Park Military Hospital as a 400-bed institution for incurables and the chronically ill.

The first Cancer Detection Clinic in Canada has been opened at the Women's College Hospital, Toronto. Dr. Elise L'Esperance, New York Memorial Hospital, officiated at its opening.

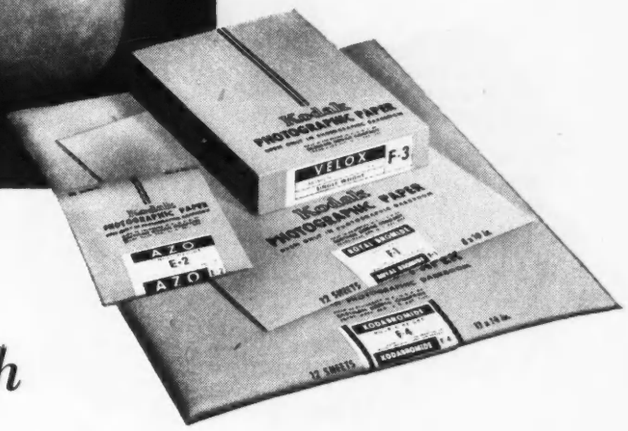
LILLIAN A. CHASE

The London Academy of Medicine held its Annual Academy Day on April 28. Medical and Surgical Clinics were conducted by Drs. Ford K. Hick, and Chas. B. Puesto, both of the University of Illinois. Luncheon was provided at the Victoria Hospital followed by a Round Table Discussion and in the evening the Annual Academy Dinner was held with Squadron Leader H. C. Forbell, R.C.A.F., as guest speaker.





Picture the patient's progress



. . . with photograph . . . after photograph

Simple then . . . to review every step . . . to present the case in its entirety for study and discussion—months, years later.

BUT RECORDS like this require photographic papers of highest quality . . . that yield prints that show every detail of the negative.

Kodak provides such photographic papers for both contact prints and enlargements, in contrast grades and speeds to suit every negative . . . with surface textures, stock tints, weights, and image tones appropriate to each print's purpose—always uniform, every sheet, every package . . . year in, year out.

For example: Kodak Azo and Kodak Velox contact papers come in five and six contrast grades respectively . . . Velox prints cold blue-black . . . Azo, cold black; Kodabromide, a general all-purpose, enlarging paper is available in four contrast grades. For further information about these and the many other Kodak Papers, see the nearest photographic dealer . . . or write Canadian Kodak Co., Limited, Toronto 9, Ontario.

Other Kodak products for the medical profession

X-ray films; x-ray intensifying screens; x-ray processing chemicals; electrocardiographic film and paper; cameras—still and motion picture; projectors—still and motion picture; photographic films—color and black-and-white (including infrared); photographic processing chemicals; synthetic organic chemicals; Recordak products.

Serving medical progress through Photography and Radiography

"KODAK" IS A TRADE-MARK

Kodak

Quebec

Le Dr Albert Jutras a été élu vice-président de la Société médicale de Montréal, remplaçant le Dr. J. E. Samson, démissionnaire.

Le 7 novembre dernier, au cours d'une réunion tenue à l'hôpital des Anciens Combattants du chemin de la Reine-Marie, il fut décidé de former une association que l'on nomma "La Société Canadienne de Chirurgie plastique". Le Dr G. E. Cloutier est le secrétaire-trésorier de cette société.

Lors de sa séance annuelle du 26 février dernier, tenue à l'hôpital Notre-Dame, le Conseil des Hôpitaux de Montréal a procédé à l'élection de son exécutif. Les officiers suivants ont été élus: président: Mr J. H. Roy, de l'hôpital St. Luc; 1er vice-président: Dr J. E. DeBelle, du "Children's Memorial Hospital"; 2e vice-président: Mr René Laporte de l'hôpital Notre-Dame; secrétaire: Dr Lorne C. Gilday, du "Montreal General Hospital"; trésorier: Dr Edmond Dubé, de l'hôpital Ste. Justine; conseillers: Dr Ernest Brunet, de l'hôpital St. Jean de Dieu et Mr H. D. Jack, du "Royal Edward Laurentian Hospital".

Le Dr Roméo Grondin, autrefois de l'hôpital St. Luc de Montréal, devient radiologiste à l'hôpital Notre-Dame de l'Espérance de St. Laurent.

Le Dr Geo. Leclerc de l'hôpital Notre-Dame a été élu "Fellow" de l'American Board of Dermatology and Syphilology.

Les Drs Wilder Penfield et Jean Saucier ont éte choisis à titre de vice-présidents pour représenter le Canada au IVe Congrès international de neurologie de Paris en 1949.

Le Dr Antonio Samson a été nommé chirurgien orthopédiste de l'American Board of Orthopedic Surgery.

Le prochain congrès de l'A.M., L.F.C. aura lieu à Ottawa-Hull les 6, 7, 8, 9 septembre 1948.

JEAN SAUCIER

Saskatchewan

The American Society of Anæsthesiologists, Inc. and Western Divisions, Canadian Anæsthetists' Society held a joint meeting in Regina on April 23 and 24. On Friday evening, those attending were guests at the regular monthly Dinner Meeting of the Regina and District Medical Society. The sessions were held at the Grey Nuns' Hospital and the General Hospital, as well as the Hotel Saskatchewan. The meeting was addressed by Dr. Ralph M. Waters, University of Wisconsin; Dr. R. C. Adams, of Mayo Clinic, Rochester, Minn.; Dr. R. A. Gordon, Toronto, Secretary-Treasurer of the Canadian Anæsthetists' Society; and John H. Hunt, Executive Secretary of the American Society of Anæsthesiologists, Inc.

The first of several district meetings to be held in May took place at Prince Albert on May 3. Dr. W. S. Kinnear and Dr. B. A. Jackson of Saskatoon presented scientific papers. The Registrar, Dr. G. Gordon Ferguson, brought the meeting up to date on provincial medical affairs.

The Regina and District Medical Society and the Department of Veterans' Affairs co-operated in conducting a refresher course in Regina from May 3 to May 8, for general practitioners. Dr. S. E. Moore was Chairman of the Monday session in General Hospital, Dr. D. E. Rodgers conducted a medical clinic, with round-table discussion led by Drs. S. Young, E. H. Duncan, E. T. French. Jr. Speakers on Monday were Drs. L. Cowan, H. J. Spooner, M. G. Israels. All speeches and sessions of the course were recorded.

Changes in the province include the appointment of Dr. J. T. MacDougall, formerly of Indian Head, to Deer Lodge Hospital in Winnipeg.

Dr. H. D. Jenner, on the staff of the T.B. Sanatorium in Prince Albert, has returned from Edinburgh with his M.R.C.P.

L. E. WELLS

General

International Postgraduate Courses on Social and Industrial Psychiatry.—The National Council for the Rehabilitation of Industrial Workers of Great Britain is holding a series of weekly postgraduate courses on social and industrial psychiatry for the following dates: June 28 to July 4; August 9 to 15; August 23 to 29; September 20 to 26. These will be held at the Roffey Park Rehabilitation Centre, thirty-five miles from London. The inclusive fee is $50.00 covering tuition, residence and social activities. Applications stating the preferred dates should be made to the Secretary, Roffey Park Rehabilitation Centre, Horsham, Sussex, England.

National Cancer Institute of Canada.—On April 8 the Board of Directors of the National Cancer Institute of Canada awarded grants in aid of Cancer Research totalling $166,000 to forty-six applicants from the various research centres throughout Canada. Two or three applications are still pending and action on these will be announced later. The successful applicants and the location of their laboratories are listed as follows: Dr. J. G. Aldous, Dalhousie; Dr. Helen I. Battle, University of Western Ontario; Dr. R. W. Begg, Dalhousie; Drs. C. H. Best and E. A. Sellers, University of Toronto; Dr. C. J. Bishop, Acadia; Dr. O. Bluh, University of British Columbia; Dr. Eldon Boyd, Queen's; Dr. A. W. A. Brown, University of Western Ontario; Dr. R. K. Brown, University of Alberta; Dr. A. Cantero, University of Montreal; Dr. Geo. Duff, University of Toronto; Dr. Lyman Duff, McGill; Dr. K. C. Fisher, University of Toronto; Dr. A. W. Ham, University of Toronto; Dr. F. R. Hayes, Dalhousie; Dr. M. M. Hoffman, McGill; Dr. H. R. Johns, Univeristy of Saskatchewan; Drs. W. V. Cone and J. Kershman, McGill; Dr. B. N. Kropp, Queen's; Dr. C. P. Leblond, McGill; Dr. J. M. Lederman, University of Manitoba; Dr. Jeanne Manery, University of Toronto; Dr. H. D. McEwen, Queen's; Dr. A. F. McKay, Queen's; Dr. D. A. McLarty, University of Western Ontario; Dr. D. Nicholson, Winnipeg General Hospital; Dr. R. L. Noble, University of Western Ontario; Dr. R. Parker, Connaught Laboratories; Dr. Dorothy Pelluet, Dalhousie; Dr. J. H. Quastel, Montreal General Hospital; Dr. H. E. Rawlinson, University of Alberta; Dr. H. V. Rice, University of Manitoba; Dr. R. J. Rossiter, University of Western Ontario; Dr. R. B. Sandin, University of Alberta; Dr. Hans Selye, University of Montreal; Dr. L. C. Simard, Notre Dame Hospital; Dr. C. E. van Rooyen, Connaught Laboratories; Dr. O. H. Warwick, McGill; Dr. J. K. Watson, University of Western Ontario; Dr. A. M. Wynne, University of Toronto.

Fellowships were awarded to Dr. S. Albert, McGill; Dr. W. B. Ayre, Boston; Dr. L. C. Coleman, Sannichton, B.C.; Mr. J. D. Hamilton, University of Western Ontario; Dr. D. W. A. Roberts, University of Toronto; Dr. R. C. Ross, McGill.

The Canada Handbook for 1948 is now available. It is as usual a profusely illustrated survey of Canada's growth and economic and cultural progress. It more than supplements the Canada Year Book and provides a most attractive birdseye view of our country. It is obtainable from the King's Printer, Ottawa for .25 cents. Postage stamps are not accepted in payment.

(Courtesy of the Candian Pacific Railway Company)

CONGRATULATIONS!

Brigadier W. P. Warner, C.B.F., D.S.C.; Major-General C. P. Fenwick, C.B., C.B.E., M.C., E.D.; and Brigadier H. M. Elder, C.B.E., D.S.O. (reading from left to right) on the occasion of their decoration by His Excellency Viscount Alexander on April 8. General Fenwick was created a companion (Military Division) of the Most Honorable Order of the Bath, and Brigadiers Elder and Warner were made Commanders of the Order of the British Empire.

Advance copies of the new British Pharmacopœia may be seen at the Food and Drug Laboratories of the Department of Health and Welfare, at the following centres: Ottawa—35 John Street; Montreal—Room 304, 379 Common Street; Toronto—59 Victoria Street; Winnipeg—Corner of Magnus and Main Streets; Vancouver—Room 504, Federal Building, 325 Granville Street; Halifax—Dominion Public Building, Bedford Row.

The copies must be consulted on the premises and cannot be loaned. The official day of publication is September 1, 1948.

BOOK REVIEWS

Child Health. Edited by A. Moncrieff, Nuffield Professor of Child Health, University of London, and W. A. R. Thomson. 254 pp., illust. 14s. Published on behalf of *The Practitioner* by Eyre and Spottiswoode (Publishers) Ltd., London, 1947.

Six chapters of this Handbook are devoted to the organization, work, and problems of Welfare Centres, Day Nurseries, School Health Services, etc., and give some inclination of the apparent trend towards socialization that seems to be taking place in the British Isles. In urban Canada, pædiatricians are more numerous per capita than in the British Isles and play perhaps a more active part in the guidance of all phases of child care than is possible in Britain. On this account the solutions of some of our Canadian problems may possibly be viewed from somewhat different angles, but this book offers very concise and exact information of great value in the child welfare work of any country.

The book is primarily compiled for the general practitioner, but the data are of considerable interest to all who are concerned with child health. It furnishes a ready and compact reference book on the present status of child welfare work in the British Isles.

Essentials of Modern Surgery. Edited by R. M. Handfield-Jones, Surgeon to St. Mary's Hospital; and A. E. Porritt, a surgeon to His Majesty the King. 1256 pp., illust., 3rd ed. $12.50. E. & S. Livingstone Ltd., Edinburgh; Macmillan Co. of Canada, Toronto, 1948.

This book is the result of an attempt to cover the whole of surgery in one volume. This means that there is of necessity a minimum of extraneous matter in the text, and one cannot expect either minute details or complete coverage of any subject. The excellence of the writing is just what one has come to expect in British texts, and the list of contributors who are authorities in their subjects, guarantees that the content is as good as the writing. This is a very satisfactory account of the fundamentals of modern surgery.

Clinical Practice in Infectious Diseases. E. H. R. Harries, Medical Superintendent, North-Eastern Hospital (London County Council); and M. Mitman, Medical Superintendent, River Hospital. 679 pp., illust., 3rd ed. $5.00. E. & S. Livingstone, Ltd., Edinburgh; Macmillan Company of Canada, Toronto, 1947.

This book gathers together a great deal of useful and interesting information about the common systemic bacterial and virus infections. The classical clinical pictures are given and these are accompanied by admirable reviews and discussion of the recent advances in the pertinent bacteriology, serology and epidemiology. To the student who finds that to understand makes learning easier and to the practitioner to whom understanding adds to the pleasure of his work, this book will have a definite appeal. The teacher, too, will find it a ready source of useful information. Combining in one book the classical knowledge of disease with its more recent advances is a very commendable thing to do. It is to be hoped that the authors will keep their contribution useful by frequent editions.

Factors Regulating Blood Pressure. Edited by B. W. Zweifach and Ephraim Shorr, Department of Medicine, Cornell University Medical College, New York, cine, Cornell University Medical College, New York. 175 pp., illust. $1.90. 1948.

In initiating a program of conferences, the first of which is reported in this volume, the Josiah Macy Jr. Foundation is undoubtedly making a major contribution to progress in medical investigation. While it is a valuable experience for the participants to discuss their findings and intentions and to be freely criticized, the record of such a conference is equally valuable for all workers in the field discussed. It is not for the new findings that may be presented that the report of such a meeting is valuable but rather for those points of "know-how" which, important though they be, are rarely published. This conference was concerned specifically with experimental renal hypertension, and the possible pressor mechanisms involved. As such the report forms a highly technical volume designed for the specialist and investigator in the immediate field.

Pharmacognosy. E. N. Gathercoal, Emeritus Professor of Pharmacognosy, University of Illinois, and Elmer H. Wirth, Professor of Pharmacognosy and Pharmacology, University of Illinois. 756 pp., illust., 2nd ed. $10.00. Lea & Febiger, Philadelphia; Macmillan Co. of Canada, Toronto, 1947.

It is quite probable that few medical men will read this book. Pharmacognosy may even be a new word to the majority of them. The identification of drug stuffs has long ceased to be a part of a physician's training. The few who will appreciate such a work will find nostalgic pleasure in meeting old friends such as Cajuput, Origanum and Zingiberis. They will also find that one of the sources of Coumarin is "sweet bed straw". Every drug in the U.S. Pharmacopœia is described and the work is right up to date. Penicillin, Streptomycin and Bacteriophage are discussed as well as Curare. It may be doubted if even a medico-legal expert would feel competent to identify the elements in a powder made of vegetable drugs. A table similar to that used in organic chemistry is given as a guide. It is an elaborate process but it can be done by an expert in pharmacognosy. The book is, of course, designed for students in pharmacy. It would be a guide to a fascinating hobby.

Diabetes Mellitus in General Practice. A. R. Colwell, Associate Professor of Medicine and Director of Medical Specialty Training, Northwestern University Medical School. 350 pp., illust. $5.25. Year Book Publishers, Inc., Chicago, 1947.

This work on diabetes mellitus has been added to the series of General Practice Manuals by the Year Book Publishers, Inc. In it the author has set forth his methods of treatment and the results of his experience with diabetes for the past twenty-five years. The book is written with a noticeable directness of style, and many controversial aspects are dealt with in a definitive way which is scarcely warranted. It contains chapters on general information, diagnosis, treatment by diet and by insulin, and complications.

Modern Drugs in General Practice. Ethel Browning, M.D., Ch.B. 231 pp., 2nd ed. $3.25. Edward Arnold & Co., London; Macmillan Co. of Canada, Toronto, 1947.

This book contains a great deal of useful information. Many of the newer drugs are dealt with, their preparations, dosage, therapeutic and toxic effects are described. The opinions advanced by the author are conservative and helpful. It is hard to understand the omission of any reference to the liver preparations when many pages are devoted to the sedative hypnotics and local anæsthetics. Too much space is given to the claims of manufacturers for their trade-marked products. On the other hand, the book gives many synonyms for the various preparations. This will be particularly helpful to the Canadian practitioner who is bewildered by not only the numerous trade-marked names under which certain drugs are sold, but also by the different official names given to these same drugs in the British and the United States pharmacopœias.

P-Q-R-S-T A Guide to Electrocardiogram Interpretation. J. E. F. Riseman, Associate in Medicine, Harvard Medical School. 84 pp., illust., 2nd ed. $3.50. Macmillan Co., New York and Toronto, 1947.

This unique little book reminds one of A. N. Whitehead's aphorism "Seek simplicity and mistrust it". It is best described as the equivalent of a student's notes taken in the course of lectures on electrocardiography. The notes are brief, they condense subjects, and one must assume the student's memory and understanding of the subject has been quite good if he is to find these notes helpful. The interpretation of electrocardiograms cannot be practised with this book alone, for it is intended only as a reminder of details that can be kept ready at hand; it is a slender volume that will fit a rather wide pocket.

BOOKS RECEIVED

Henry Sewall, physiologist and physician. G. B. Webb and D. Powell. 191 pp., illust. $2.75. The Johns Hopkins Press, Baltimore, 1946.

Junior Speaks Up. I. R. Abrams, Associate attending physician, Cook County Children's Hospital, Chicago. 164 pp. $2.50. Macmillan Co., New York and Toronto, 1948.

Medical Annual 1947. Edited by Sir Henry Tidy and A. Rendle Short. 464 pp., illust. $6.25. John Wright & Sons Ltd., Bristol; Macmillan Co. of Canada, Toronto, 1947.

Mycopathologia. Vol. IV, No. 2. Edited by R. Ciferri and P. Redaelli. Illust. Dr. W. Junk, Publisher, N. Z. Voorburgwal 64, Amsterdam-C. January, 1948.

Physiological Effects of Time Schedule Work on Lumber-Workers. N. P. V. Lundgren. 137 pp. Swed. Crowns 12. Acta Physiologica Scandinavica, Stockholm 1946. Distr. by Affarsekonomi, Stockholm, 3, Sweden.

Proceedings of a Conference on Industrial Ophthalmology. Sponsored by the Columbia University College of Physicians and Surgeons in co-operation with the National Society for the prevention of blindness. 291 pp., illust. Columbia University Press, New York, 1947.

ANNUAL MEETING
Canadian Medical Association
June 21 to 25, 1948
Toronto, Ontario

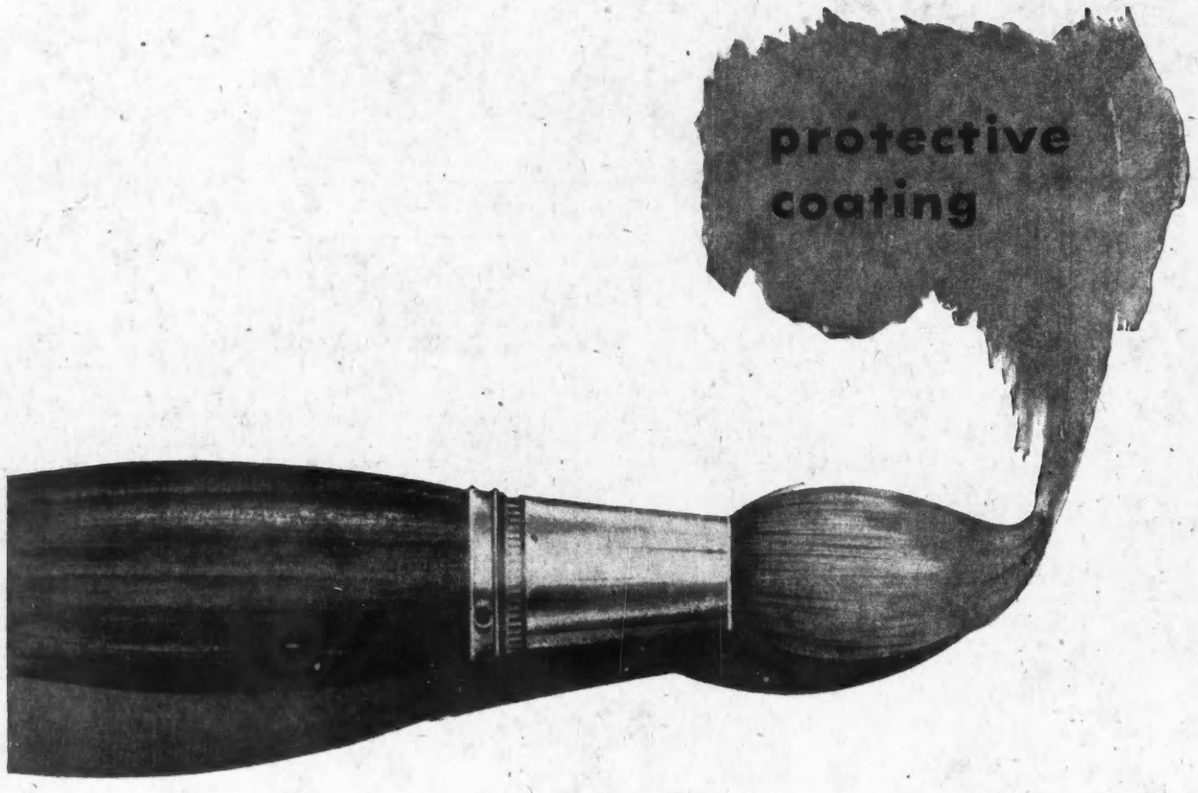
INDEX NUMBER

The Canadian Medical Association Journal

Vol. 58 JUNE, 1948 No. 6

Contents

Published Monthly by THE CANADIAN MEDICAL ASSOCIATION, 3640 University Street, Montreal
[PRICE SEVENTY-FIVE CENTS PER COPY]
Printed in Canada by MURRAY PRINTING COMPANY, LIMITED, 192 SPADINA AVENUE, TORONTO 2-B.



KAOSORB

(Pectin and Kaolin Compound, Lilly)

'Kaosorb' is a nonchalky, attractive kaolin mixture with a creamy, heavy-bodied smoothness. This preparation has considerable appeal to the patient. The ample kaolin content functions as an adsorptive and effectively produces a protective coating that soothes inflamed intestinal mucosa.

'Kaosorb' is indicated for the supportive treatment of diarrhea and inflammation associated with enteritis, gastritis, colitis, and other intestinal infections or intoxications.

FORMULA:

An aromatized aqueous suspension containing in one fluid ounce:

Pectin	4 1/2 grs.
Kaolin	90 grs.
Zinc Phenolsulfonate	1 1/8 grs.

ELI LILLY AND COMPANY (CANADA) LIMITED
TORONTO, ONTARIO

PROPHYLAXIS OF ASTHMATIC ATTACKS

"FELSOL POWDERS offer a remedy in Asthma well adapted for the prophylaxis of cases. With relief of broncho-spasm an attack is abolished and with prevention of spasm Asthma is avoided.

"When taken in time FELSOL will modify very considerably an impending attack of Asthma.

"Without morphia or other narcotic FELSOL achieves relief with perfect safety even in cardiac cases.

"Careful graduation of dosage in early cases of ASTHMA yields a high percentage of successful results—prevention of spasm abolishes the tendency in early cases."

Physicians' samples and literature available on request to
Sole distributors for Canada:

Felsol POWDERS *for* **ASTHMA**

THE ANGLO-FRENCH DRUG COMPANY,
209, ST. CATHERINE STREET EAST, MONTREAL

BRITISH FELSOL COMPANY LTD., 206/212 St. John St., London, E.C.1. **Telegrams: Felsol Smith, London.**

BACKGROUND

The use of cow's milk, water and carbohydrate mixtures represents the one system of infant feeding that consistently, for over three decades, has received universal paediatric recognition. No carbohydrate employed in this system of infant feeding enjoys so rich and enduring a background of authoritative clinical experience as Dextri-Maltose.